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No. 1

ROENTGENOLOGIC FINDINGS IN THE LUNGS OF VICTIMS OF THE COCOANUT GROVE DISASTER*†

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THE clinical features of the respiratory tract injuries among the victims of the Cocoanut Grove disaster as observed at the Boston City Hospital have been described in detail elsewhere.¹ The severity of the damage to the respiratory tract in these cases was graded roughly according to the clinical manifestations as follows:

Grade	Clinical Manifestations
0	No signs or symptoms referable to the respiratory tract.
1	Signs and symptoms limited to the upper respiratory passages, including mild laryngitis.
2	Evidence of involvement of the trachea and bronchi or abnormal signs in the lungs other than those of frank consolidation.
3	Dyspnea, cyanosis, wheezing or transient stridor or frank signs of consolidation.
4	Evidence of extensive pulmonary involvement or of obstruction to the airways necessitating tracheotomy or resulting in severe asphyxia.

The severity of the respiratory damage classified in this way was shown to be correlated fairly closely with the extent of the surface burns. In individual cases, however, there were wide discrepancies but most of

these could be explained by unusual circumstances. For example, in some of the patients who died with severe respiratory tract damage but with few or no surface burns, it was ascertained that they were stampeded early and their bodies were protected from the flames by the bodies of others. They nevertheless continued to inhale the hot and irritating fumes. In others who succeeded in extricating themselves from the building or in those who covered their mouth and nose, there was little or no respiratory tract involvement but they sustained burns which were often quite extensive.

The deaths were of two general types and were associated either with (1) burns involving 30 per cent or more of the body surface or (2) severe respiratory tract injuries which resulted in obstruction to the air passages. There were only 2 recoveries among 30 patients with respiratory symptoms of Grade 4 severity.

The signs and symptoms referable to the respiratory tract were interpreted as consistent with the effects of laryngotracheobronchitis of varying extent and severity.

* From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), the X-ray Department, and the Burn Assignment to the Surgical Services, Boston City Hospital and the Department of Medicine, Harvard Medical School, Boston, Massachusetts.

† The work described in this paper was done, in part, under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University.

The autopsy findings suggested further that the clinical manifestations in the severe cases had resulted from varying degrees of obstruction due to the pseudomembrane and the viscid exudate which covered the tracheobronchial tree and often extended down to the small bronchioles. These gave rise to patches of atelectasis in some parts of the lung while in other parts there were areas of emphysema and dilated bronchi due to air trapped beyond the obstructing lesions. In addition, the autopsies revealed thrombosis of pulmonary vessels with infarcted areas in the lungs of patients who died within the first three or four days, and patchy or confluent lesions of bronchopneumonia in some of those who died after that time. As might be expected, these changes gave rise to rather variable and often extensive and bizarre changes in the roentgenographic appearance of the lungs.

Similar but less extensive findings resulting from exposure to noxious gases have been described before.^{2,3} A thorough roentgenologic report of the pulmonary lesions in the cases from the Cocoanut Grove fire which were studied at the Massachusetts General Hospital has been given by Schatzki.⁴ The clinical features of those cases were described by Aub *et al.*⁵ Since Schatzki's descriptions cover most of the changes observed in the cases studied at the Boston City Hospital, they will be summarized here and will serve as a background for the report of roentgen findings observed. The latter will be correlated, in a general way, with the clinical signs and symptoms and with the autopsy findings. Selected roentgenograms in some of the severe cases will serve to illustrate the various types of abnormalities that were seen.

Schatzki found roentgen changes in the lungs of 22 of 35 patients examined. The first roentgenograms showed flame-like areas radiating asymmetrically from both hila with scattered bands and lines, as well as large homogeneous and small miliary areas of increased density. From the further development of these lesions and from the autopsy findings, Schatzki felt that

interference with aeration due to complete or partial obstruction of the bronchi, particularly the smaller ones, was the cause of most, if not all of the visible pulmonary changes.

In chest roentgenograms of 2 autopsied cases dead on arrival he found extensive, diffuse, poorly defined haziness extending throughout most of both lung fields. This was interpreted as characteristic of pulmonary edema and that was confirmed by the autopsy findings. Both of these cases showed high concentrations of carbon monoxide in their blood. The roentgenograms in 3 other patients who died in the hospital all showed areas of emphysema and patches of atelectasis. In 1 of them there was evidence of pulmonary edema in the last roentgenogram; another showed a peculiar mottling and the third showed a round area of localized emphysema resembling trapped air such as that which is sometimes seen in children (pneumatocele). Autopsies in these 3 cases showed tracheobronchitis and bronchiolitis with patchy atelectasis and emphysema, some pulmonary edema as well as localized areas of atelectasis and hemorrhage which may have represented early infarctions.

Interestingly enough one of the 13 patients with negative roentgen findings died of respiratory embarrassment some hours after the negative roentgenogram was obtained. Furthermore, all but two of the surviving roentgenologically negative patients had râles on physical examination on one or more occasions.

Schatzki's descriptions of the various types of roentgenographic lesions may be summarized briefly. *Atelectasis* was recognized in several forms. Sudden massive lobar atelectasis was seen in only 1 case, and the gradual development of complete collapse of both lower lobes was observed in another. More commonly there were smaller areas represented by triangles, or by bands, discs, or even fine lines of increased density which ran horizontally, obliquely and, in the lower lobes, even vertically through the lung fields. The oc-

currence, in the same roentgenograms, of compensatory emphysema, elevation of the diaphragm and displacement and contraction of the hilar shadows on the side where the changes were extensive was taken as proof of the atelectactic origin of the shadows. Lateral shift of the mediastinum was rarely seen due to the fact that there was bilateral involvement in most cases.

Emphysema, lobar and lobular in distribution, was seen in several patients during various stages. Schatzki was able to demonstrate them best on roentgenograms taken in expiration, indicating the presence of trapped air. There was usually some atelectasis in the same lungs. One case of persistent lobar emphysema was also described. *Miliary mottling* of both lungs with individual lesions measuring 2 to 6 mm. in diameter was observed in only 2 fatal cases. These shadows were not adequately explained but were thought to be due to small areas of atelectasis or possibly to small plugged bronchi. A homogeneous ground-glass appearance of a large portion of one lobe or one lung without decrease in size of the involved part was noted in the early roentgenograms in 3 survivors. Since these cleared rapidly they were interpreted as representing fluid in partially atelectatic lungs, the so-called "drowned lungs." *Pulmonary edema* was identified in only the 2 fatal cases already mentioned. *Infarcts* of the lungs, though seen in the autopsies, were not recognized roentgenologically except in the later roentgenograms of some of the severely burned cases in which they were obviously connected with thrombophlebitis.

In the cases admitted from the Coconut Grove disaster to the Boston City Hospital roentgenograms were not made until about thirty-six hours after the fire except in a few instances. At that time a roentgenogram of the chest was taken at the bedside on almost every patient who was still in the hospital. Additional roentgen examinations of the chest, varying from one to five in number, were made in 57 of the cases during the remainder of the hospital stay. In

some of these cases roentgenograms were taken both in inspiration and in expiration. Roentgenograms of the chest were also included as part of the follow-up examination of those who returned to the hospital for this purpose.

After all of the roentgenograms were reviewed, the extent of the abnormal findings in each case was graded according to an

TABLE I

CORRELATION OF SEVERITY OF RESPIRATORY INVOLVEMENT AS OBSERVED CLINICALLY WITH THE DEGREE OF PULMONARY CHANGES OBSERVED ROENTGENOGRAPHICALLY

Grade of Respiratory Involvement (Clinical)	Degree of Pulmonary Changes Observed in Roentgenograms					Total (cases)
	0	1	2	3	4	
0	8 ¹	2	0	0	0	10 ¹
1	8	14 ¹	6	0	0	28 ¹
2	0	8 ¹	8	1 ¹	0	17 ²
3	0	2	10	7 ¹	1 ¹	20 ²
4	0	0	2 ²	3 ³	7 ⁴	12 ⁵
Total (cases)	16 ¹	26 ²	26 ²	11 ⁵	8 ⁵	87 ¹⁵

Six cases are included in which roentgenograms were taken at other hospitals to which the patient was removed within 36 hours after the fire.

44 cases (51%) had same rating clinically and roentgenographically.

29 cases (33%) had a clinical rating 1 grade higher than the roentgen rating.

10 cases (11%) had a roentgen rating 1 grade higher than the clinical rating.

4 cases (5%) had a clinical rating 2 grades higher than the roentgen rating.

Superscripts represent fatal cases.

arbitrary scale from 0 to 4. Those with the most extensive changes were classified as Grade 4 and those with only minor abnormalities in the roentgenograms were classed as Grade 1. A correlation of the roentgen changes classified in this manner with the severity of the symptoms in each case is shown in Table I. There was a fairly close correlation between the severity of the respiratory symptoms and the extent of the roentgen changes. Wide discrepancies were very few. In about one-third of the cases the severity of the respiratory symptoms was somewhat greater than was indicated by the roentgen changes in the lungs, but



FIG. 1. Case 1. *A*, second day: extensive mottling especially in the right upper lung field; patchy areas of emphysema, and diffusely diminished aeration of the left lower lung. *B*, eleventh day: considerable clearing with diffuse emphysema in the upper lung fields.

The patient lost consciousness early at the fire. On admission she had regained consciousness but was restless and coughing. A few crepitant râles were heard at the base of the right lung and there were cardiac signs of mitral stenosis. Burns involved mostly the face, shoulders and hands—estimated 7 per cent. She rapidly developed hoarseness, dyspnea and her cough markedly increased; she began to raise sputum which was thick, mucoid and black at first and then became blood streaked. When *A* was taken there were showers of loud crepitant râles throughout both lungs and the patient was very dyspneic. The râles decreased gradually during the next few days and only a few were heard over the left lower lobe when *B* was taken. The lungs had cleared completely but there was still some cough and hoarseness when the patient was discharged on the sixteenth day. Three months later she was still having intermittent slight hoarseness and cough but she had improved considerably. One year later her general condition was excellent, she had no more cough but did have a chronic post-nasal discharge which began after the fire. She became hoarse only after using her voice excessively. Roentgen and physical examination of her chest were completely negative.



FIG. 2 (See opposite page for legend.)

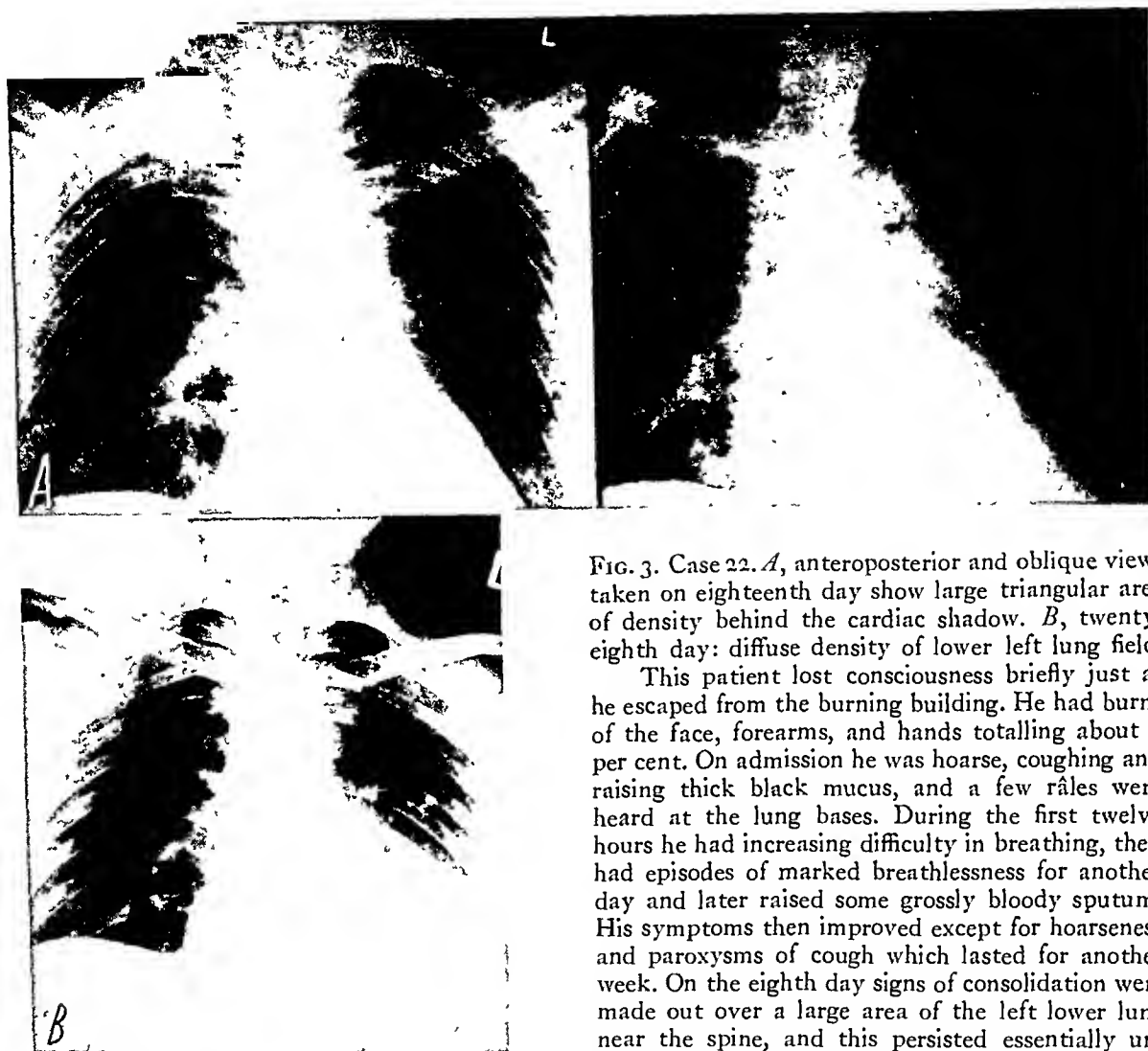


FIG. 3. Case 22. *A*, anteroposterior and oblique views taken on eighteenth day show large triangular area of density behind the cardiac shadow. *B*, twenty-eighth day: diffuse density of lower left lung field.

This patient lost consciousness briefly just as he escaped from the burning building. He had burns of the face, forearms, and hands totalling about 6 per cent. On admission he was hoarse, coughing and raising thick black mucus, and a few râles were heard at the lung bases. During the first twelve hours he had increasing difficulty in breathing, then had episodes of marked breathlessness for another day and later raised some grossly bloody sputum. His symptoms then improved except for hoarseness and paroxysms of cough which lasted for another week. On the eighth day signs of consolidation were made out over a large area of the left lower lung near the spine, and this persisted essentially unchanged during the next three weeks until the pa-

tient was transferred to a Naval hospital. In routine chest roentgenograms the area of density was obscured by the cardiac shadow but oblique views showed a dense triangular area extending from the hilum to the diaphragm as seen in the figure. During the fourth week there was an episode of fever associated with extension of the signs throughout the left lower lobe as shown in *B*. The lung has cleared slowly and the patient has been returned to active duty but details of his course after leaving the hospital could not be ascertained.

FIG. 2. Case 8. *A*, second day: diffuse emphysema; patchy atelectasis in lower right and soft mottling in lower left lung field. *B*, sixth day: residual patchy atelectasis in right lower lung field.

The patient was overcome inside the burning building and regained consciousness while being brought to the hospital. His burns involved the entire face and both ears—total 4 per cent. On arrival he was very hoarse and coughing and numerous râles were heard throughout both lungs. At the time when the earlier roentgenogram was taken he was having dyspnea, occasional episodes of stridor and some pain in the right chest and was raising green sputum containing leukocytes, epithelial cells and type 3 pneumococci. Improvement in symptoms began on the next day and the signs in the lungs cleared progressively so that at the time of the later roentgenogram there were only a few crepitant râles at the bases and occasional scattered high pitched musical râles throughout both lungs. These were still present at the time of discharge three weeks later. He was returned to active duty in the Navy and when last heard from, two years after the fire, he was free of symptoms except for occasional cough productive of a small amount of sputum.

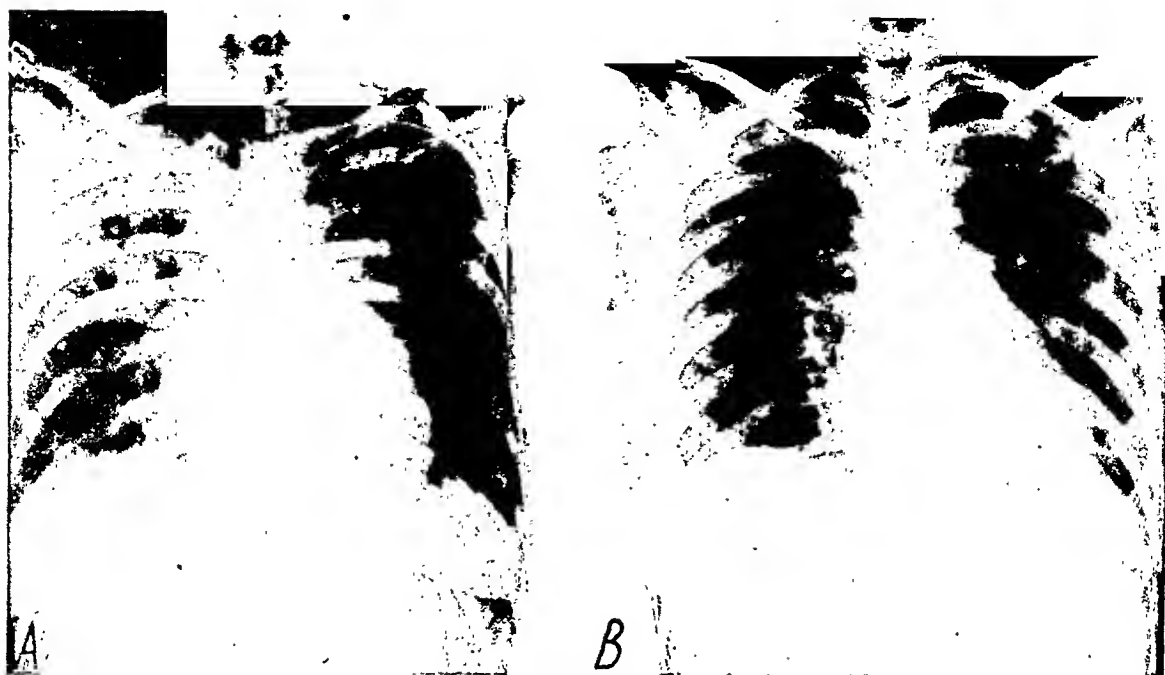


FIG. 4. Case 47. *A*, second day: extensive densities mostly in the right upper lung field with some emphysema (trapped air) in that area. *B*, tenth day: almost complete clearing.

The patient was knocked down and trampled and lost consciousness before she could attempt to escape. She suffered no external burns. On admission she was hoarse and coughing and râles were heard over the right chest. The lungs cleared somewhat for a while but then the patient began to have dyspnea, wheezing, a feeling of constriction in the chest and stridor. A tracheotomy was contemplated but not done when laryngoscopy revealed singed vocal cords. At the time of the earlier roentgenogram the patient was very hoarse and there were showers of crepitant râles at the lung bases and scattered high pitched musical râles, especially in the left lung. The coughing and hoarseness had improved considerably, the crepitant râles had cleared but the high pitched squeaks persisted and the patient was still having difficulty in taking a deep breath at the time when the later roentgenogram was taken. She continued to have some cough and some dyspnea on exertion for the first three months after discharge but after eight months there was only occasional cough and her general condition has been good. Physical examination and roentgenogram of the chest after eight months were entirely negative.

the reverse was found to be true only in a few cases. It is not unlikely that greater discrepancies might have been noted if roentgen examinations had been done earlier and more frequently.

The roentgen changes observed at the Boston City Hospital were essentially the same as those described by Schatzki, but some of them appeared to be more frequent and more extensive than those encountered at the Massachusetts General Hospital. In particular, the diffuse miliary type of mottling in large areas of the lung was seen more frequently in the early films. In some cases the individual lesions had a nodular appearance which varied considerably in density. The mottling extended throughout both lung fields in some of the severe

cases, while in others it was limited to one or two lobes. Some patchy or confluent areas of density, probably those of bronchopneumonia, were also noted. This was particularly marked in the roentgenogram taken shortly before death in Case 107 as shown in Figure 11. Enlargement of the hilar shadows with increase in density and accentuation of the bronchial markings were quite frequent. In some cases, dilated and thickened bronchi could be seen extending down to the dome of the diaphragm.

Emphysema was evidenced by patchy areas of increased radiance, but in several cases this was extensive and predominantly unilateral and there was enlargement of the thorax on that side. Subcutaneous emphy-



FIG. 5. Case 53. The fine areas of density, especially in the left lower lobe, which were present on the second day (A) have largely cleared and there is some increase in the bronchial markings on the seventeenth day (B).

The patient lost consciousness shortly after inhaling some of the smoke but he sustained only minor burns of the face. He had a chronic productive cough and a history of occasional asthmatic attacks. On admission he was coughing, his throat was diffusely inflamed and there were numerous râles throughout his lungs. His cough increased during the following day and he developed progressive dyspnea, restlessness and air hunger. The next morning there were signs of consolidation in the right lower lobe. These signs and symptoms cleared up dramatically during the day after a violent coughing spell following which the patient coughed up what looked like a fibrinous cast of a bronchus containing sheets of epithelial cells. The earlier roentgenogram was taken shortly after this episode and there were only crepitant râles heard at the bases at that time. There were occasional episodes of mild dyspnea during the next two days and the breath sounds were diminished at the lung bases on some examinations. Improvement continued and the lungs were clear and the patient symptom free when the later roentgenogram was taken. When last seen several weeks later he had remained well and without residual symptoms. Physical examination and roentgenogram of the lungs at that time were negative except for emphysema.

sema was noted in the roentgenograms taken after tracheotomy and this usually persisted for several days. It was limited mostly to the supraclavicular regions but in one instance extended into the axillae.

Atelectasis manifested by the various types of density described by Schatzki was seen in most of the positive roentgenograms. In addition, there were several cases in which the findings were interpreted as those of partial atelectasis of most of one lobe or one lung. The involved areas showed a more or less uniformly diminished radiance with elevation of the diaphragm, contrac-

tion of the intercostal spaces, and, in some instances, by an appreciable though not marked shift in the mediastinal contents to the affected side. Massive and complete atelectatic collapse involving most of the left lower lobe was noted in only 1 instance, Case 22, Figure 3, and in that case it persisted for several weeks. A large area of consolidation extending beyond the atelectasis appeared at the end of the fourth week in this case.

Pulmonary edema was not made out in any roentgenograms, but no postmortem roentgen examinations were made at this



FIG. 6. Case 70. Diffuse irregular densities and some patchy emphysema on the second day (A); most of this has cleared by the sixth day (B) but there is some diminished aeration of the left lower lung.

The patient lost consciousness after inhaling much smoke. His surface burns were limited to the face. On admission he was stuporous, very hoarse, coughing vigorously and having some difficulty in breathing. At that time he was slightly cyanotic and coarse rhonchi were heard throughout both lungs and finer crepitant râles at the bases. During the next two days the patient was quite restless and dyspneic and he had noisy respirations with occasional stridor. He coughed violently and raised scanty amounts of dark mucoid sputum. At the time of the earlier roentgenogram there were fine râles at the lung bases and some scattered musical râles and the patient was having episodes of asthmatic-like breathing. After that the patient began to improve and the lungs gradually cleared but hoarseness persisted until discharge. When last seen two years later, the lungs were clear on physical and roentgen examination and he had remained free of respiratory symptoms.



FIG. 7 (See opposite page for legend.)

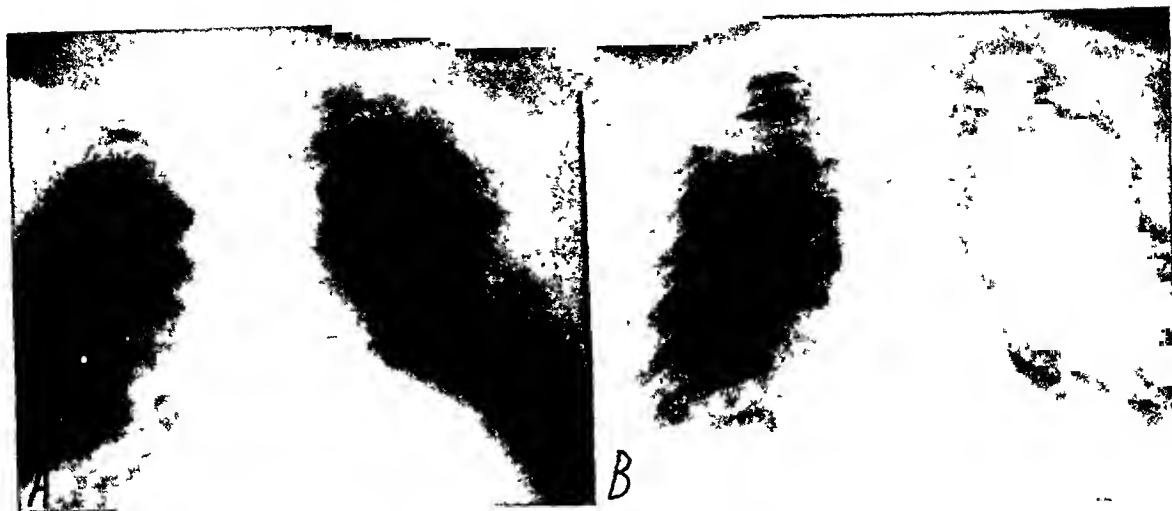


FIG. 8. Case 91. *A*, second day: tracheotomy tube in place; edema of soft parts and subcutaneous emphysema in supraclavicular and axillary regions; partial atelectasis of lower lobes with patchy densities in the right lower and emphysema in upper lung fields. *B*, eleventh day: tube still in place with similar but less marked changes.

The patient had temporary loss of consciousness before he got out of the burning building and again while being taken to the hospital. His burns involved the face and hands—about 6 per cent. There was a long history of morning cough productive of mucoid sputum. On admission he was hoarse, coughing violently and raising black, tenacious sputum. He soon developed increasing dyspnea and stridor and a tracheotomy was done on the following afternoon. Obstructive symptoms continued and necessitated frequent suction which yielded copious amounts of bloody mucoid material. The earlier roentgenogram was taken on the day after the operation when the lungs were filled with rhonchi and crepitant râles. Episodes of obstruction requiring suction continued for several days and the lung signs during that time were quite variable. When the later roentgenogram was taken there were only a few râles heard at the lung bases posteriorly and the breath sounds were diminished over these areas. The tube was removed a week later and the patient had a small hemoptysis on the following day. Thereafter, his symptoms improved rapidly. When last seen nearly two years after discharge he was in excellent health and had been carrying on his usual rather strenuous activities and having no more cough and sputum than he did before the fire. No abnormalities were made out on physical examination or roentgenogram of his chest at that time.

FIG. 7. Case 90. *A*, second day: tracheotomy tube in place; mottled densities especially in upper lung fields; patchy atelectasis and emphysema. *B*, sixth day: tube out and lung fields cleared considerably. Right-sided cardiac enlargement—same in both roentgenograms.

The patient became unconscious while still in the Melody Lounge and, except for a brief interval soon after she was carried out through a window, she remained in this state until a few hours after her arrival at the hospital. There was a history of bronchial asthma but no recent attacks. Burns totalling about 5 per cent involved the face, a shoulder, a hand and a leg. The patient was irrational for several hours but dyspnea was first noted after about twelve hours and then progressed rapidly along with marked stridor until a tracheotomy was done. For several hours thereafter she continued to be restless and dyspneic with spells of breathlessness which were relieved by suction. When *A* was taken there were loud rhonchi and crepitant râles throughout both lungs. The patient began to improve rapidly, however, and breathed comfortably with the tracheotomy tube plugged, so it was removed a few hours later. Some dyspnea and wheezing continued and high pitched musical and some crepitant râles were heard in the lungs, mostly at the bases, for several days. During the next two years her general condition has remained good. She has some morning cough and sputum which occasionally is blood streaked but there have been no asthmatic attacks. Physical examination and roentgenograms of the lungs in inspiration and expiration were entirely normal.



FIG. 9. Case 92. The tracheotomy tube is in place and subcutaneous emphysema in the supraclavicular areas are present in both roentgenograms; the marked densities seen on the second day (*A*) have largely cleared by the sixth day (*B*).

The patient inhaled a good deal of smoke and lost consciousness just before reaching an exit but she sustained no surface burns. On admission she had regained consciousness and was having some respiratory distress and numerous rhonchi and high pitched musical râles were heard throughout both lungs. During the next few hours her dyspnea increased markedly and she finally developed air hunger which necessitated a tracheotomy for relief. *A* was taken on the following day when the patient was still having considerable respiratory difficulty and there were numerous râles and rhonchi in both lungs at that time. She began to improve two days later and at the time of the later roentgenogram (*B*) was breathing much more comfortably but there were still many crepitant scattered musical râles. Except for a few choking spells due to plugging of the tracheal tube she improved steadily, and the tube was removed on the sixteenth day. Hoarseness, cough and a few rhonchi were still present when the patient was discharged one week later. When last heard from two years later she was entirely well except for a slight residual cough productive of very small amounts of mucoid sputum.

hospital in cases dead on arrival. This finding may also have been missed in fatal cases in which the last roentgenograms were taken some time before death. Extensive pulmonary edema, however, was not found, even in the autopsies of these cases. There was evidence of extensive and marked edema of soft parts, particularly of the face and neck in some of the cases as illustrated in Figure 14.

A summary of the numbers of cases in which each of the various types of roentgen changes were noted, and the relevant clinical findings are shown in Table 11. As might be expected from the nature of the lesions, the clinical signs and symptoms were generally more frequent and more severe than

was indicated by the roentgen changes. The discrepancies between the severity of the respiratory symptoms and roentgen changes in the lungs, on the one hand, and the extent of the surface burns, on the other, are seen from Table 11 and have been referred to previously.

In general, the more extensive roentgenographic lesions had largely cleared before the end of the first week. Small areas of atelectasis and patches of emphysema with some increases in the hilar shadows and of the bronchial markings persisted longer in some of the cases. The area of massive and complete atelectasis in Case 22 persisted unchanged for several weeks. In a few instances, there were marked fluctuations

TABLE II

SUMMARY OF RELEVANT ROENTGENOLOGICAL AND CLINICAL FINDINGS CLASSIFIED ACCORDING TO THE EXTENT OF THE ROENTGEN CHANGES SEEN IN THE LUNGS

Grade of Roentgen Changes	0	1	2	3	4	Total
Number of Cases	11	26	25	11	8	81*
Roentgen Findings						
<i>Mottling:</i> coarse	—	1	6	8	7	22
fine	—	18	18	2	1	39
mostly unilateral	—	11	12	2	—	25
bilateral	—	8	12	8	8	36
<i>Emphysema:</i> patchy	—	14	19	9	5	47
diffuse†	—	1	5	2	3	11
<i>Atelectasis:</i> patchy	—	10	17	4	4	35
diffuse† (partial)	—	15	8	6	4	33
massive (complete)	—	—	—	1	—	1
<i>Consolidation</i> (mostly patchy)	—	—	—	3	2	5
<i>Increased hila:</i> unilateral	—	9	21	—	—	30
bilateral	—	11	2	11	8	32
Clinical Findings						
<i>Symptoms:</i> hoarseness	3	15	24	10	7	49
cough	6	22	25	11	8	72
dyspnea	—	6	12	10	8	36
wheezing	—	—	9	5	6	20
stridor	—	—	9	7	7	23
<i>Physical signs:</i> lungs clear	6	—	—	—	—	6
crepitant râles	4	19	23	9	8	63
musical râles	4	13	15	11	8	51
diminished breathing	1	9	11	3	2	26
consolidation	—	—	4	2	3	9
<i>Extent of surface burns:</i>						
0-5%	6	16	12	3	3	40
6-10%	2	7	5	3	2	19
11-20%	2	0	2	1	1	6
21% or more	1	3	6	4	2	16
<i>Deaths</i>	1	2	2	5	5	15

* Six cases transferred to other hospitals within the first 36 hours are excluded from this table.

† Most of these had patchy areas as well.

in both physical and roentgen findings as might be expected. This was particularly striking in some of the cases with tracheotomy and in others who had repeated episodes of respiratory obstruction and required frequent suction to relieve their symptoms. Some of the roentgenograms in the 3 patients who recovered following tracheotomy, namely Cases 90, 91 and 92, are shown in Figures 7, 8 and 9, respec-

tively. Most of the clearing in these cases had taken place within two or three days after the operation. The subcutaneous emphysema is also noted in these roentgenograms. Reproductions of roentgenograms taken in some of the other cases are also shown in the other figures and the relevant clinical findings are given in the accompanying legends.

The findings in some of the fatal cases



FIG. 10. Case 104. Second day: in both lung fields—more on the left—there are numerous areas of soft density but the extreme bases are clear.

The patient had apparently lost consciousness at the fire. She had burns of the face, arms and hands—total about 7 per cent. On admission, she was restless, excited and having respiratory difficulty, and coarse rhonchi were heard throughout both of her lungs. She continued to be restless and had episodes of excitement associated with stridor and air hunger. Showers of coarse crepitant râles were heard at both lung bases at the time of this roentgenogram. The patient obtained only slight and temporary relief from oxygen given under positive pressure. About thirty-six hours after this roentgenogram was taken the patient died during an episode of air hunger which was not relieved by tracheotomy. Just prior to the operation the lungs were hyperresonant throughout and only a few high pitched squeaks were heard.

At autopsy the trachea showed irregular areas of necrosis and some hemorrhagic foci. The mucosa of the larynx, trachea and bronchi was moderately injected and covered with a thick gray-black mucoid material. Some of this material also filled the smaller bronchi and was dislodged only with difficulty. The lungs showed scattered sunken bluish-red areas of consolidation within which there were obstructed bronchi and bronchioles. There was also some diffuse edema.



FIG. 11 (See opposite page for legend.)

FIG. 12. Case 124. Second day: extensive mottled densities and patchy atelectasis in the lower lung fields and emphysema in the uppers.

The patient lost consciousness while trying to escape from the fire and was stuporous and in shock on arriving at the hospital. He had severe burns of the face, neck and extremities—total about 10 per cent. On admission he was having spells of violent coughing and there were loud tracheal râles, a few scattered inspiratory wheezes and some fine crepitant râles at the bases. He developed marked air hunger and more profound shock after the first twelve hours. Suction was required frequently to relieve the obstruction which was partly due to moisture in the upper respiratory passages. The patient died eight hours after this roentgenogram was taken.

Autopsy showed edema and redness of the epiglottis, trachea and major bronchi which were covered with thick greenish and pinkish material but there was no underlying ulceration. In the smaller bronchi and bronchioles there were yellowish friable casts, and the underlying mucosa and part of the muscle walls were necrotic. There was a widespread early bronchopneumonia with polymorphonuclear cells and necrotic debris in the lumens of some of the bronchi and also some destruction of alveolar walls and early abscess formation.



are of interest. In Case 107 (Fig. 11), the first roentgenogram was taken after a tracheotomy had been performed and during a period when the patient was relatively free of obstructive symptoms. The lung fields in this roentgenogram were relatively clear. The patient had recurrent episodes of

obstruction which were only partially and temporarily relieved by suction and she later developed signs of consolidation in the lungs. Roentgen examination at this time showed some confluent bronchopneumonia. An incidental finding was that of a megacolon which was noted in both roent-

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FIG. 11. Case 107. The tracheotomy tube is in place in both roentgenograms which also show the distended megacolon; many areas of marked density in the left cardiophrenic angle and some patchy atelectasis in the left lower lung on the second day (A) and more extensive and softer density especially in the right lung on the sixth day (B).

The patient was in shock and having some respiratory distress at the time of admission when rhonchi and wheezes were heard throughout her chest. She had deep burns on about 12 per cent of the body including her face, neck and extremities. Her breathing became increasingly difficult and a tracheotomy was done after eighteen hours. Thereafter, she had frequently recurring obstructive episodes requiring suction and this produced moderate amounts of viscid dark bloody material. She obtained some relief from oxygen under positive pressure after some of these episodes. At the time of the earlier roentgenogram there were numerous rhonchi and crepitant râles throughout both lungs. On the fifth day there were signs of consolidation in the left upper lobe and the râles persisted and increased in the rest of the lung. The patient died on the day after the later roentgenogram was taken.

At autopsy there was an opaque yellowish-gray pseudomembrane covered with dirty viscid mucoid material beginning in the larynx above the vocal cords and extending well into the primary bronchi. The smaller bronchi were dilated down to the diaphragmatic surface and there was some necrosis of their walls. Some bronchioles were filled with fibrin plugs. The lungs showed scattered areas of emphysema, atelectasis and consolidation and some confluent bronchopneumonia. The roentgen finding of a megacolon was confirmed.

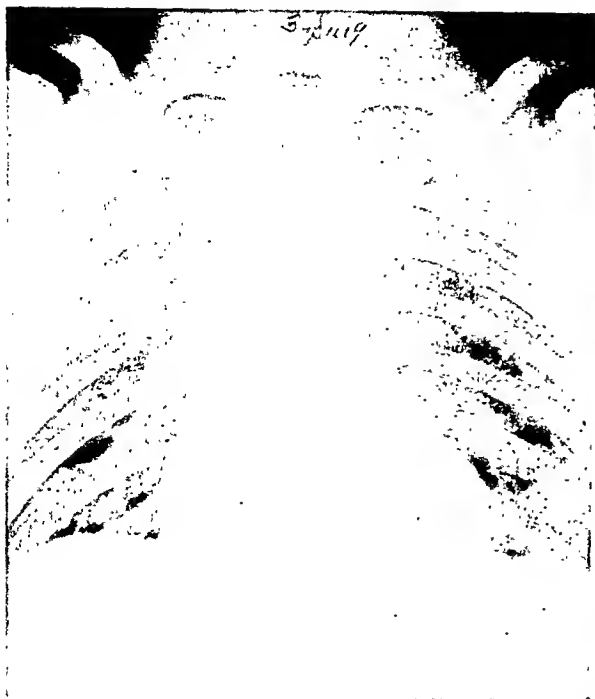


FIG. 13. Case 125. Second day: diffuse haziness of most of both lung fields with scattered areas of density of various shape, particularly in the lower portions; widened right supracardiac area.

At the time of admission the patient was semi-comatose, in shock, hoarse, coughing and having some difficulty in breathing, and coarse râles were heard throughout both lungs. Burns were severe and extensive and involved about 45 per cent of the body, including the face. During the first twelve hours respirations became increasingly noisy and labored and dark mucus was removed by suction. Black and later bloody mucus was raised by the patient or removed by suction frequently thereafter. There were scattered râles at the lung bases posteriorly at the time this roentgenogram was taken but breath sounds over these areas were subsequently diminished. Dyspnea persisted and progressed and the patient died on the sixth day.

At autopsy there was a soft edema of the lower pharynx and small submucosal hemorrhages and hyperemia of the mucosa of the epiglottis, larynx, trachea and bronchi which were covered with a film of thin mucopurulent material. The lungs contained multiple petechial and large confluent hemorrhages over the posterior and lateral surfaces and many areas of superficial atelectasis. There was somewhat generalized emphysema of the upper lobes and a large infarcted area in the left lower lobe with other scattered areas of infarction, atelectasis and trapped air as well as fibrin thrombi filling many small bronchi and bronchioles the walls of which showed considerable necrosis.

genograms. These findings were confirmed at autopsy and the characteristic severe laryngitis, tracheitis and bronchitis with areas of atelectasis and emphysema were also present.

In Case 104 (Fig. 10) the roentgenogram was taken about thirty-six hours before



FIG. 14. Case 6. *A*, taken on the second day, shows the marked swelling of the face and neck which had almost entirely receded when *B* was taken on the sixth day.

death, which resulted from acute respiratory obstruction that was not relieved by tracheotomy. Examination of the lungs just prior to the operation showed them to be hyperresonant throughout and only high pitched musical sounds were heard. Autopsy in this case showed acute tracheitis,

laryngitis, bronchitis and bronchiolitis with surrounding small foci in the alveoli. There was some rather diffuse atelectasis and edema.

In Case 128 there were no significant roentgen findings. The patient had extensive burns and died during the twelfth week. His lungs were entirely clear at autopsy. In a second patient with extensive burns (Case 109) there were only small areas of atelectasis and emphysema and some increase in the hilar shadow in the roentgenograms taken during the first week. The patient had only mild and transient dyspnea and a slight cough. No definite abnormal physical findings were made out in her chest. The patient died after five months and the lungs were found to be entirely normal at autopsy.

In Cases 106 and 120, moderate changes (Grade 2) were made out in the roentgenograms taken on the second day. The former died about twelve hours later during a sudden attack of acute obstruction which was not relieved by tracheotomy. Her lungs were resonant throughout and only a few high pitched râles were heard at the time. There was no autopsy in this case. In Case 120, death occurred about thirty-six hours after the roentgenogram was taken. Numerous crepitant râles were heard throughout the lungs in this case. Autopsy showed hemorrhagic acute laryngitis, tracheitis and bronchitis with focal areas of hemorrhagic consolidation in the lungs. The remaining fatal cases all had more extensive roentgenographic changes and all showed patchy areas of atelectasis and emphysema in addition to the lesions in the larynx, trachea and bronchi. There were some areas of bronchopneumonia in those dying after the fourth day and these areas were confluent and almost lobar in distribution only in Case 107.

Follow-up roentgen examinations in inspiration and expiration were done in many of the patients who had moderate or extensive changes in the early roentgenograms. No residual abnormalities were de-

tected in roentgenograms of any of these cases six months to two years after the fire.

SUMMARY

The significant roentgenographic changes observed in the cases admitted to the Boston City Hospital from the Cocoanut Grove fire have been reviewed and related to the clinical and autopsy findings. The roentgen changes were essentially similar to those described by Schatzki and were consistent with the lesions found at autopsy. Most of them could be ascribed to atelectasis and emphysema resulting from a severe membranous laryngotracheobronchitis with obstruction. The clinical symptoms and physical signs were frequently more severe and extensive than the changes visible in the roentgenograms. No residual roentgen changes in the lungs were noted in the recovered cases in which there was an opportunity for follow-up.

The authors are indebted to Dr. Patrick F. Butler, Director of the X-ray Department, for his constant interest and encouragement, to Drs. C. C. Lund and F. H. L. Taylor, the responsible investigators of the Burns Project, to the members of the surgical staff of the Boston City Hospital who permitted us to study their cases and to Dr. Timothy Leary for the pathological data.

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PULMONARY CHANGES IN CARBON TETRACHLORIDE POISONING*

By LIEUTENANT (JG) CHARLES MOREAU THOMPSON (MC) USNR

RECENTLY a series of 20 cases of carbon tetrachloride poisoning occurring on a submarine were treated at this Naval Dispensary. Of the cases, 3 were critically ill and 1 died. During their illness roentgenograms of the chest were made. Some very unusual changes were noted that are deemed worthy of reporting. It was impossible to make a complete survey of the literature at this outlying base, but in none of the papers reviewed was mention made of roentgen changes in the lung fields.

Carbon tetrachloride is an excellent solvent for grease, fat, tar and oils, and used not uncommonly for cleaning purposes. Aboard the submarine the solvent was used in a confined compartment for cleaning the deck and bulkheads. When exposed to high temperature carbon tetrachloride can break up into phosgene and hydrochloric acid, both of which are pulmonary irritants. However, it is the opinion of the author that the men were poisoned by the direct inhalation of the fumes. The metal plates being cleaned were not hot, and none of the men initially had any symptoms of phosgene inhalation. The pulmonary changes were not discovered until nine days after exposure.

CLINICAL MANIFESTATIONS

The course of the cases reported below is similar to that in the literature except for a few variations. Of the 20 cases, 4 were severely ill, presenting a typical toxic nephrotic syndrome as evidenced by puffiness and swelling of the soft tissues of the face, hands, and feet. They had retention of nitrogenous waste products in the blood stream and evidence of real kidney damage. Due to limited laboratory facilities, complete blood and urine studies were not possible. The fatal case developed acute

pulmonary edema while apparently on the road to recovery. Because of this, roentgenograms were made of the chest of each patient. Findings varying from mild prominence of all lung markings to complete consolidation of all five lobes were observed. Enlarged hilar shadows, peribronchial infiltration and a change in the size and configuration of the heart were also noted. The patient with pulmonary symptoms had extensive consolidation of both lung fields and died despite all supportive treatment.

CASE REPORTS

The 4 serious cases are outlined in brief, along with the gross and microscopic findings of the lungs in the fatal case.

CASE 1. P. DeS., male, white, aged twenty-four. Patient admitted with backache, malaise and vomiting. He had severe oliguria with four plus albuminuria. For six days he was acutely ill at which time he appeared to be improving and seemed to be the least ill of the critical patients. Suddenly the patient developed acute respiratory distress with deep cyanosis and hemoptysis. Respirations were 34 per minute with a pulse rate of 120 per minute. Roentgen examination of the chest was made. Temperature was normal and remained so. Course râles and wheezes were heard over both lungs. The patient became rapidly worse, respirations reached 40 per minute and pulse 140 per minute. Because of the marked cyanosis and air hunger he was placed in an oxygen tent. He began to cough up large amounts of red frothy sputum. Patient died about thirty hours after the onset of his pulmonary symptoms.

Autopsy and Microscopic† Findings of the Lungs.* **Gross:** There were petechial hemorrhages on the smooth glistening surfaces of the lungs. The lungs were heavy and, with the

* Autopsy performed by Captain H. Salm, M.C., A.U.S.

† Microscopic examination performed by Colonel F. H. Foucar, M.C., A.U.S.

* The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or as reflecting the views of the Navy Department or the Naval Service at large.

exception of parts of the lower lobes, were considerably consolidated. The cut surfaces of each were dark red and very wet. The mucosa of the tracheobronchial tree was a dark purplish red. *Microscopic:* There was marked venous capillary congestion and edema. The alveoli were filled with granulocytes, numerous erythrocytes and many swollen lightly pigmented macrophages. Findings—congestion and edema; pneumonia, acute, hemorrhagic in type.



FIG. 1. Case I. Roentgenogram of the chest reveals a homogeneous density involving the lung fields. There is only a small amount of aerated lung at the right apex and at the left base. The cardiac silhouette is obscured by the consolidation in the lung fields. There is no definite evidence of free fluid in either pleural space. (This is not an underexposed film.)

CASE II. A. B., male, white, aged twenty-three, admitted with nausea, vomiting, albuminuria, and oliguria. Albuminuria persisted for fourteen days. Shortly after admission facies became bloated, edematous and waxy. He was critically ill for two weeks with nausea, vomiting with hematemesis, oliguria and anorexia. He was fed intravenously and convalescence was slow. Roentgen examination of the chest was first made on the seventh hospi-

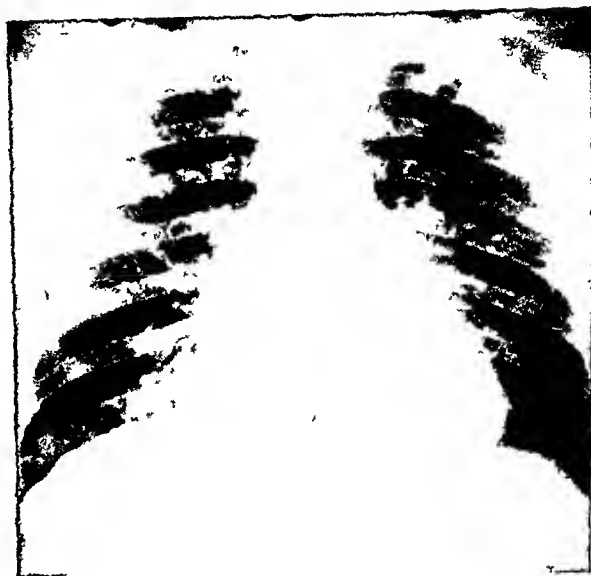


FIG. 2. Case II. Roentgenogram of the chest reveals an increase in the hilar and lung markings. The markings fan out into the periphery of the lung fields. In the mid-portion of the right lung field there is a linear line of increased density probably due to interlobar pleural thickening or focal atelectasis. The cardiac silhouette is slightly globular in shape.

tal day. In spite of roentgen evidence there were no physical or clinical findings in the chest. Two days later a roentgenogram of the chest was essentially negative. Patient was discharged on the thirty-second hospital day.



FIG. 3. Case II. Re-examination of the chest three days later reveals marked resolution of the prominent lung markings previously described.

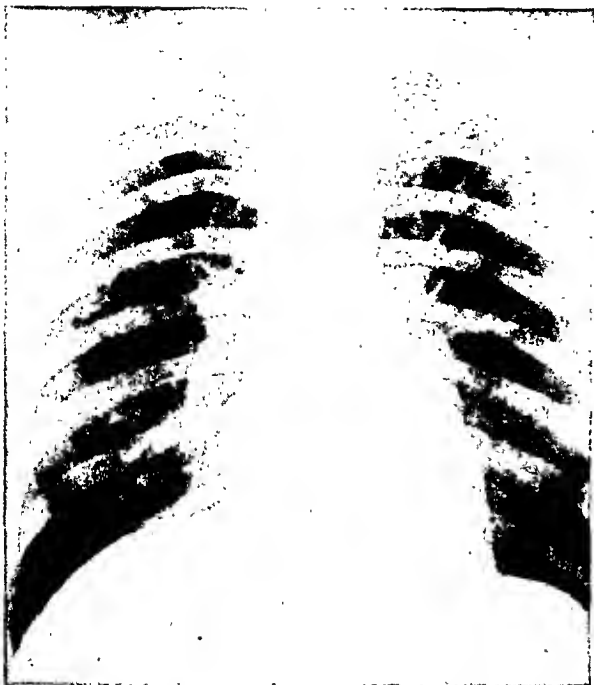


FIG. 4. Case III. Roentgenogram of the chest reveals an increase in the prominence of the hilar markings and root shadows. The cardiac silhouette appears normal. Re-examination three days later revealed the lung fields to be normal.

CASE III. J. B., male, white, aged twenty-two. Patient admitted with severe vomiting and low back pain. Oliguria and albuminuria were severe and persisted for a week. Shortly after admission he developed large flame-like

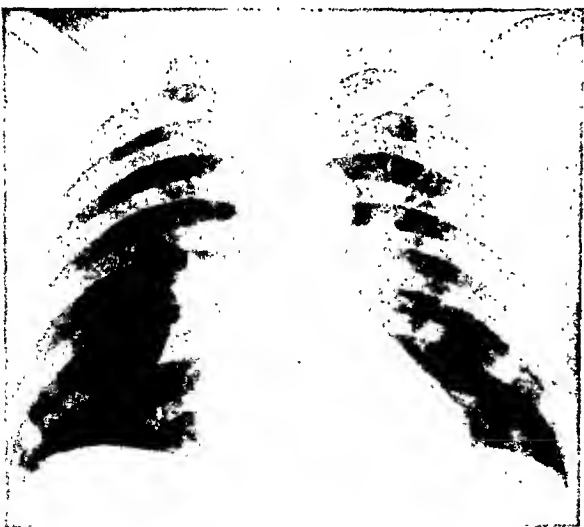


FIG. 5. Case IV. Roentgenogram of the chest reveals prominence, enlargement and increased density in both hilar areas with fine linear shadows radiating out into the lung fields.

subconjunctival hemorrhages. Roentgenogram of the chest was made on the seventh hospital day. He was the least ill of the 3 living patients. Discharged on thirty-second hospital day.

CASE IV. L. J., male, white, aged twenty-four, admitted with severe prostration, vomiting and generalized muscular pain. There was anuria for five days followed by oliguria and albuminuria. He developed subconjunctival hemorrhages and marked photophobia on the

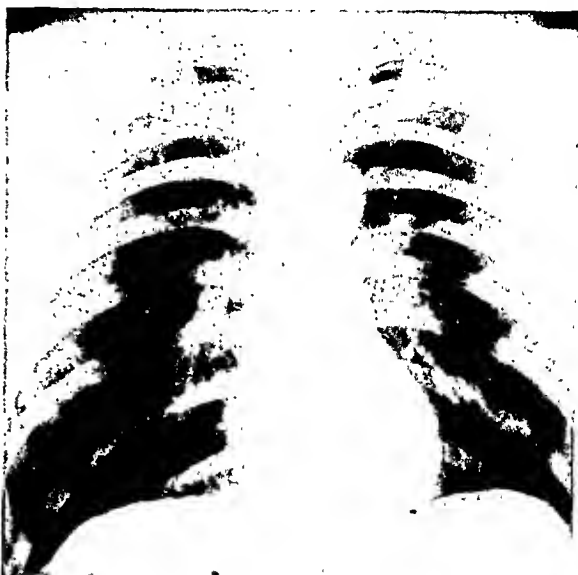


FIG. 6. Case IV. Re-examination of the chest one week later reveals marked improvement of the hilar and lung infiltration previously described. The lung fields now appear normal. It is noted that there has been marked change in the configuration of the cardiac silhouette. The heart on this examination is not as globular in shape. Part of this change in the cardiac silhouette may be attributed to the greater descent of the diaphragm and better aeration of the lungs.

second hospital day. The soft tissues of the face became edematous and waxy. He had nitrogenous retention. The patient was unable to tolerate food by mouth for two weeks and required intravenous feeding. Roentgenogram of the chest on the seventh hospital day showed marked prominence and infiltration of both hilar areas. A second examination one week later revealed a decrease in the pulmonary infiltration and a change in the configuration of the cardiac silhouette. Convalescence was slow and he was discharged on the thirty-fourth hospital day after the most stormy course of the living patients.

SUMMARY

Four in a series of twenty cases of poisoning by inhalation of carbon tetrachloride fumes have been presented along with roentgenograms of the chest. The clinical course of each case and the autopsy findings in the fatal case were consistent with those described in the literature. Pulmonary roentgenographic changes were discovered late in the course of events. The changes varied from consolidation of all five lobes to mild increase in all lung markings. In one case there was a change in the configuration of the cardiac silhouette between examinations. Only the fatal case had symptoms and physical findings of organic change in the lung fields. In the other three patients the predominating symptoms were gastrointestinal, followed by renal shut-down.

It is interesting to note that the amount of change on the roentgenograms of the chest was directly proportional to the severity of the patients' clinical illness; i.e., the more ill the patient, the greater were the findings on the roentgenogram. Perhaps pulmonary roentgen changes may be used as criteria in the prognosis and morbidity of

cases with carbon tetrachloride poisoning.

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ESOPHAGOBRONCHIAL FISTULA THROUGH AN ESOPHAGEAL DIVERTICULUM

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ESOPHAGOBRONCHIAL fistulae are not exceedingly rare but the occurrence of such a fistula through an esophageal diverticulum has apparently been reported only once. It is for this reason and for the therapeutic possibilities of the cauterization method of Clerf³ in the treatment of bronchoesophageal fistulae that our case is presented.

CASE REPORT

Mrs. J. M. (admission No. 114114), female, married, white, aged forty, entered Mount Sinai Hospital on September 21, 1941, with the chief complaint of "hemorrhage through the nose and mouth." She stated that such an episode first occurred one afternoon in 1940 while hurrying to board a streetcar, the blood

loss being about one-half pint. When the patient returned home, she felt faint, nervous, restless and dyspneic. The bleeding gradually subsided but less severe attacks of bright red bleeding occurred subsequently.

The patient awoke during the night of September 9, 1941, and regurgitated about a "pint" of dark clotted "chunks" of blood, and on the following day, she vomited bright red blood. She also complained of severe epigastric, right shoulder, and neck pains, the complaints being intensified while eating. She noticed that there was an increase in eructations, but they were not of the sour type. The patient claimed she was able to drink milk but could not tolerate fried or greasy foods or cream. The stools appeared darker than usual but not black.

The past history included "flu" in 1918, a hysterectomy in 1932 and a ventral hernia repair in 1940. The patient had 5 miscarriages and 5 living children, having married at the age of fifteen.

Physical Examination. On entrance to the hospital this obese, white, pale female was in acute pain. There was marked right upper abdominal tenderness which was increased during deep inspiration but no rigidity or spasm was found. The liver, kidneys and spleen were not palpable. An incisional hernia was recognized in the lower abdomen. No definite abnormal physical findings were elicited in the heart or lungs. The blood pressure was 92/60, pulse 84. The impression on admission was (1) bleeding gastric ulcer, (2) chronic cholecystitis with cholelithiasis.

Laboratory Data. The admission red blood count was 4,250,000 per cu. mm.; hemoglobin 13 grams; white blood cell count 11,800 with a normal differential count. The Kline test was reported as negative. A catheterized urine specimen showed no definite abnormalities.

Roentgen examination of the chest on September 22, 1941, by means of roentgenoscopy showed no gross abnormality in the heart, lungs, mediastinum or diaphragm. Upon administering a thick barium sulfate mixture,



FIG. 1. Spot roentgenogram taken during barium meal examination on September 22, 1941, shows a tract (T), probably fistulous, extending posteriorly and inferiorly into the right lung region from diverticulum (D) in lower half of esophagus.

the esophagus was opacified and a diverticulum measuring approximately 3 cm. in diameter was visualized in the lower half. A tract leading posteriorly from the diverticulum for about a distance of 1 inch was observed (Fig. 1). Whether there had been a communication between the esophagus and bronchial tree was not stated at that time, but review of the roentgenograms, however, leads one to believe that there must have been a communication. In the region of the diverticulum considerable spasm was noted. There was no evidence of neoplastic involvement. The stomach and duodenum showed no abnormality.

Course. On September 23, 1941, two days after admission, esophagoscopy was performed by Dr. John D. Steele and revealed the following: "At a point approximately 10 cm. above the cardia, considerable thin, purulent secretions were seen coming from the right wall of the esophagus. After aspiration of these secretions, the diverticulum was easily seen. The opening of the diverticulum was approximately 1 cm. in diameter. The diverticulum was approximately the size of a small olive and was lined with normal mucosa. The orifice of the fistulous tract was easily seen in the distal wall of the diverticulum. This orifice was circular and was approximately 3 mm. in diameter. There was no evidence of malignant change at any point."

Treatment consisted of bedrest, sedation, antispasmodics and a bland ulcer diet. The patient was discharged after a hospital stay of only three days.

Follow-Up Record. Except for occasional episodes of slight bleeding, the patient's general condition was good until July 10, 1942, when she again had a massive hemorrhage and was taken to the Milwaukee County Emergency Hospital. One week later she was discharged.

This patient was readmitted to Mount Sinai Hospital on January 26, 1943, with a six day history of chills, fever, cough, hemoptysis, emesis, and pain in the interscapular, left anterior chest and epigastric regions. In addition, she complained of burning on urination and noticed foul smelling urine. The patient appeared acutely ill and was expectorating thick, tenacious, bloody sputum. Examination of the heart was essentially negative and the blood pressure was 130/80. The pulse was rapid and weak, the rate being 120. Percussion of the chest revealed dullness in the left base.



FIG. 2. Esophagram made September 2, 1944, shows the esophagobronchial fistula. The fistulous tract is demonstrated between the esophageal diverticulum (D) and the bronchial tree (B).

Bronchial breathing and moist, loud, crackling râles were heard in this area but wheezes were perceived over both lung fields. Tenderness was elicited in the right upper quadrant of the abdomen but no abdominal masses were palpable. Some fever was present, the temperature on admission being 101.2° F. The diagnosis was lobar pneumonia. Chemotherapy in the form of sulfathiazole was administered and the temperature fell to normal on the second day. The temperature remained normal thereafter and the patient was discharged after a hospital stay of nine days.

About one and a half years later, or on August 25, 1944, the patient entered the hospital after she developed rather acutely, dyspnea and cough, followed by episodes of regurgitation and abdominal distention. The patient appeared slightly cyanotic, somewhat clammy and was distended. Percussion of the heart revealed suggestive enlargement to the left. The heart tones seemed weak and distant but no murmurs were heard. The blood pressure reading was 166/90, pulse was 94, and the temperature was 98.2° F. The abdomen, chiefly the left upper quadrant, was distended and presented a tympanitic note to percussion.

The impression gained was an acute gastrectasis. An electrocardiogram showed no evidence of myocardial involvement. The sedimentation rate was normal and the white blood cell count



FIG. 3. Posteroanterior projection after ingestion of barium meal (September 2, 1944) shows filling of esophageal diverticulum and right main bronchus.

was 8,200. Morphine was administered and Wangensteen suction was instituted. Within twenty-four hours the distention had disappeared and the patient was free of symptoms. On the third day the patient was dismissed.

Roentgen examination of the esophagus and chest as a clinic patient on September 2, 1944, revealed the following: A diverticulum of the esophagus was opacified by the barium mixture and measured 3.5 cm. in diameter (Fig. 2). The diverticulum was situated posteriorly and approximately in the middle of the lower half of the esophagus. A fistulous tract was visualized which extended from the posteroinferior aspect of the esophageal diverticulum to a right lower lobe bronchus. The right main bronchus was filled shortly thereafter (Fig. 3) and the patient proceeded to expectorate the opaque medium. The right lower bronchi showed some saccular dilatation.

Preliminary examination of the chest showed prominence of the lower portion of the right hilar shadow. A few bronchopneumonic areas were also noted in the right lower lung medially.

In view of the usual poor outlook for such a patient, it was agreed that some therapeutic measure or measures would have to be in-

stituted in an attempt to seal off the communication between the esophagus and bronchial tree. The patient was therefore readmitted to the hospital on October 24, 1944, for esophagoscopy and cauterization of the fistulous tract. This was attempted according to the method of Clerf and was performed by Dr. John D. Steele as follows: "The 9 by 45 esophagoscope was easily passed into the esophagus through the right pyriform sinus. The esophagoscope was first advanced to the cardia and then brought back along the right lateral wall of the esophagus until the diverticulum was encountered, as previously approximately 10. cm. above the cardia. The opening of the diverticulum into the esophagus was approximately 1.5 cm. in diameter. The diverticulum tapered down over a distance of approximately 2 cm. At the distal end of the diverticulum a circular opening approximately 3 mm. in diameter was present (Fig. 4). The mucosal lining of the diverticulum was normal in appearance. On inserting the aspirator through the opening at the end of the diverticulum the patient coughed violently, undoubtedly indicating that the aspirator had entered the bronchus. The aspirator could not be passed for more than a distance of 0.5 cm. beyond the visible portion of the opening. A small amount of bleeding followed passage of

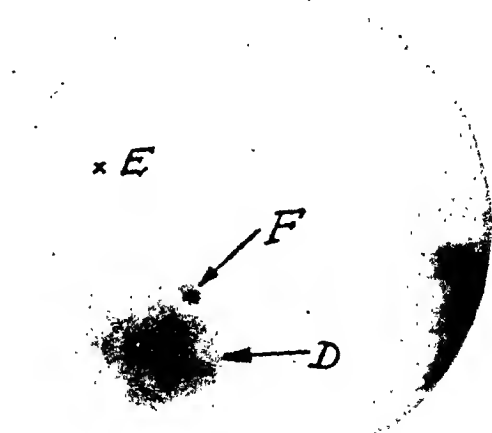


FIG. 4. Drawing of the esophagoscopic findings of Dr. John B. Steele on October 24, 1944. The esophageal diverticulum (D) is represented by the darkly shaded area and the fistulous opening (F) is demonstrated by the ring-like area. The lightly shaded portion is the wall of the esophagus (E).

the aspirator through this opening. The end of an applicator to which fused sodium hydroxide had been applied was then introduced into the mid-portion of the diverticulum and allowed to remain in place for exactly two minutes. On withdrawal of the applicator it was noted that considerable reaction had taken place, the mucosa lining the entire diverticulum now being bluish black in color and somewhat edematous. A swab soaked in boric acid solution was applied to this area. A small stomach tube was then inserted into the stomach through the nose."

Tube feeding was carried on for the following two days but the patient could not tolerate the stomach tube any longer. A soft diet was prescribed on the third postoperative day. The patient was discharged on November 2, 1944, but she had many episodes of hemoptysis in the interval. The patient was quite weak but showed no evidence of secondary anemia.

Esophagram on December 12, 1944 (Fig. 5) still showed the esophagobronchial fistula but the diverticulum was approximately one-half the original size. The patient has to date refused further treatment.

Comment. One can only postulate or theorize on the formation of the fistula in our patient. We believe it is fair to assume that the fistula was due to a ruptured gangrenous diverticulitis. Mediastinitis, pleuritis, pneumonitis and abscess formation probably followed. Rupture of the abscess into the bronchus then resulted in the esophagobronchial fistula.

The apparent failure of the one-stage cauterization in our case might be due to one or more factors. Perhaps the diameter of the communication or tract was too great to expect complete closure after just one cauterization. We believe that failure of complete closure of the tract was, at least in part, due to the fact that the patient pulled the stomach tube out after two days. The patient refused to have the tube reinserted.

DISCUSSION

Lahey⁶ states that the presence of an esophageal diverticulum was first recognized in 1764 by Ludlow at postmortem examination. Diverticula of the esophagus are ordinarily classified into pulsion and

traction types. The pulsion diverticula are divided further into the pharyngo-esophageal and supradiaphragmatic forms. The pharyngo-esophageal diverticulum is attributed to a congenital weakness of the wall between the oblique and transverse fibers of the cricopharyngeus muscles. Congenital weakness of the muscle fibers is also said to be the cause of the supradiaphragmatic or "epiphrenial" diverticula. Diverticula occurring below the tracheal bifurcation are usually in the middle of the lower half of



FIG. 5. December 12, 1944. Esophagram shows reduction in size of esophageal diverticulum after cauterization therapy on October 24, 1944. The fistulous tract is evidently narrower.

the esophagus.¹⁰ The pulsion diverticulum is more common in males than in females. The supradiaphragmatic type of pulsion diverticulum is rare, Lahey reporting only 4 cases up through the year 1940.

The traction diverticulum results from an inflammatory process in the adjacent tracheobronchial lymph nodes or mediastinal pleura with the production of cicatrization which tends to pull the esophagus out in a lateral or anterior direction. These occur chiefly at the level of the tracheal bifurcation. When the pulsion factor is added to traction diverticula, the latter become larger and rounded. Early in the develop-

ment of the traction diverticula, there is supposedly no muscular atrophy.

As with esophageal diverticula, the literature contains numerous reports of esophagobronchial fistulae. In most instances these fistulae have resulted from cancer of the esophagus, tuberculous periadenitis, syphilis of the esophagus, a congenital abnormality or a foreign body in the esophagus.⁷ By far the most frequent etiologic factor is esophageal cancer, and significant reports include those by Clerf³, Clerf, Cooley and O'Keefe,⁴ Drew and Ormerod,⁵ Allen,¹ and Brown.² In 1930 Sigora⁹ reported a case of esophageal diverticulum which perforated into the pleural cavity with the development of an empyema. The cause for the traction diverticulum was not known.

Pape⁸ in 1934 presented a case report of a chronic esophagobronchial fistula through an esophageal diverticulum. This patient had two large and two small traction diverticula with a lower small one perforating into a right lower bronchus. The right lower lobe in this case showed signs of an old healed tuberculosis with evidence of calcification. This patient was a sixty year old white male who for two years complained of pain in the upper abdomen which was transmitted to the right chest. Other symptoms included acid belches, nausea and occasional emesis of tasteless liquids. The therapy instituted consisted of advising the patient to lie on the side opposite to that of the diverticulum in order to impair the passage of food particles into the sac. The patient was also advised to eat thick pasty foods which would not pass into the diverticulum as easily as fluids might. Eighteen months after instituting this regimen, there was noted a decrease in complaints with a narrowing of the fistulous tract as well as an associated weight gain.

Diverticula of the esophagus are usually incidental findings during roentgen examination of the gastrointestinal tract. Unless an inflammatory process is present, they probably do not give rise to any symptoms.

The first complaint in a pulsion diverticulum is usually a disturbance in swallowing. Pulsion diverticula present symptoms which are related to food decomposition. Due to stasis in the sac over a long period of time, the patient regurgitates the contents of the diverticulum during the night or with change in position from the erect to the recumbent. In the case of traction diverticula, there may be no symptoms because the orifice is supposedly in a more dependent position than the sac and there is no problem of emptying. Even in the recumbent position there should be little if any difficulty. Traction diverticula, at least early in their development, contain a muscular coat and are therefore capable of contraction. Contents are therefore less likely to stagnate in such diverticula. Symptoms may accompany even such diverticula if active inflammatory changes are present. Partial obstruction due to spasm will give rise to difficulty in swallowing and even pain.

The symptoms of a simple esophagobronchial fistula consist essentially of inability to swallow food or liquid without initiating a violent episode of coughing or choking. There may be expectoration of sputum mixed with food. Hematemesis and hemoptysis can also occur. Retrosternal pain might be caused or aggravated by food intake. Interestingly enough, pain in the upper abdomen radiating to the right chest or shoulder occurred in Pape's case and in our patient. In the latter this pain was overshadowed by the hemorrhages. Nevertheless, this complaint was of sufficient concern for the examining physician to consider gallbladder disease.

ROENTGEN ASPECTS

Diverticula of the esophagus are in most instances first discovered by means of roentgen examination. The roentgen examination is often not very simple, especially if there is an associated inflammatory process. In any event, it is essential to examine the patient in all positions, including the

recumbent and even Trendelenburg position. Often it is necessary to vary the viscosity of the barium sulfate mixture in order to visualize the diverticulum. Other factors which might prevent filling of the diverticulum are debris in the diverticulum, occlusion of the neck of the diverticulum by an inflammatory process, and so forth.

The pure traction diverticulum, before the pulsion factor is added, will probably not be visualized unless the patient is examined in the recumbent or Trendelenburg position. The sac or fundus of the diverticulum is situated above the neck and, therefore, unless the fundus is placed in a dependent position in relation to the neck, the diverticulum might not be opacified. If pulsion diverticula are not completely filled by food or liquid and if the neck of the diverticulum is not occluded, they will be easily visualized. Contraction of the diverticulum is indicative of the presence of muscular fibers in the wall of the diverticulum. The traction diverticula are more apt to show evidence of contraction.

Roentgen visualization of esophagobronchial fistulae can be accomplished by means of esophagography or bronchography. Bronchography with the aid of iodized oil is probably preferable to esophagography if barium sulfate mixture is used in the latter. The barium sulfate mixture might cause serious sequelae but no deleterious effects were noted in our case. The roentgen findings can be confirmed by esophagoscopy or bronchoscopy. These methods offer further opportunity to determine etiology by virtue of the facts that direct visualization is possible and that biopsy can be obtained.

TREATMENT

The cauterization method of therapy employed in our case was devised by Clerf who in 1933 reported a case of bronchoesophageal fistula treated with 30 per cent silver nitrate. This material was applied to the esophageal end of the fistula through an esophagoscope. The patient was then fed

via a Rehfuß tube. Several weeks later, the orifice of the fistula appeared to have been obliterated. Clerf, Cooley and O'Keefe in 1943 reported 2 cases in which esophagoscopy application of sodium hydroxide crystal fused on a curved metal applicator was used with satisfactory results. Pape noted that his patient showed a decrease in complaints and that the fistulous tract was narrowed following such treatment. Whether the added factor of a diverticulum between the esophagus and air passages directly modifies the results obtained with Clerf's cauterization method as compared with the good results in simple bronchoesophageal fistulae is difficult to state. Beneficial effects have been noted following one cauterization but complete cures might require more than one application of caustic material in those cases where a diverticulum is present or in those instances where the fistulous tract is quite large.

The cauterization method, in our opinion, holds promise for cure of esophagobronchial fistulae. On the basis of our limited experience and review of the scant literature on the subject, it becomes evident that several factors must be considered and certain precautions taken. The application of the caustic must be carefully timed. A lengthy application is probably more harmful than a short one; too extensive or prolonged cauterization might result in erosion of a neighboring blood vessel. Following the cauterization it is important to put the esophagus at rest. This can be accomplished by inserting a stomach tube which should be left in situ for probably at least two weeks. Antispasmodics should be administered, and parenteral feedings are valuable adjuncts. Coughing should be prevented as much as possible by the administration of drugs such as codeine.

SUMMARY

A case of esophagobronchial fistula occurring at the site of an esophageal diverticulum is presented. The treatment of such

ment of the traction diverticula, there is supposedly no muscular atrophy.

As with esophageal diverticula, the literature contains numerous reports of esophagobronchial fistulae. In most instances these fistulae have resulted from cancer of the esophagus, tuberculous periadenitis, syphilis of the esophagus, a congenital abnormality or a foreign body in the esophagus.⁷ By far the most frequent etiologic factor is esophageal cancer, and significant reports include those by Clerf³, Clerf, Cooley and O'Keefe,⁴ Drew and Ormerod,⁵ Allen,¹ and Brown.² In 1930 Sigora⁹ reported a case of esophageal diverticulum which perforated into the pleural cavity with the development of an empyema. The cause for the traction diverticulum was not known.

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SUMMARY

A case of esophagobronchial fistula occurring at the site of an esophageal diverticulum is presented. The treatment of such

lesions according to the cauterization method of Clerf is discussed and the result of single cauterization of an esophagobronchial fistula through an esophageal diverticulum is described.

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TRUE PERICARDIAL DIVERTICULUM*

REPORT OF A CASE, WITH SAFE OPERATIVE REMOVAL

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HISTORY AND PATHOLOGY

PERICARDIAL diverticulum was first described in 1837 by Hart,¹ in the *Dublin Journal of Medical Science*. One hundred years later, Cushing,² in a comprehensive review, listed a total of 40 cases. Thirteen other cases have appeared in the literature since 1937, a total of 53.

In recent years, a very sharp and clearcut distinction has been made between two groups of these cases. First, there is the larger group of encapsulated pericardial effusions, bearing the same relationship to the pericardium as a loculated empyema does to the pleura. These "inflammatory diverticula" or "pseudodiverticula" occur in the pathogenesis of tuberculous pericarditis, rheumatic pancarditis and syphilitic cardiovascular disease. The second group, the so-called "congenital diverticula," occur in the absence of any other cardiac or pericardiac pathologic condition. Haas states that formation of such a diverticulum occurs at a point of weakness in the parietal pericardium, where the fibrous layer goes out along the great vessels. He describes three points of predilection; the base of the aorta high on the right side, the junction of the superior and inferior venae cavae on the right, lower down, and on the left, at the junction of the pulmonary veins. This group might well be labeled "true pericardial diverticula," so that their radical difference from encapsulated pericardial effusion in respect to pathogenesis, appearance, and especially prognosis may be firmly established.

True diverticula are apparently the less common type; of the total of 53 cases reported, 38 (72 per cent) are encapsulated pericardial effusions; several case reports in the remaining group do not give sufficient

information to classify them. No case of true pericardial diverticulum, proved by operation or autopsy, has appeared heretofore in the American literature.

CASE REPORT

The patient, female, aged fifty-five (Unit No. 340540) was first admitted to the Massachusetts General Hospital on February 2, 1942, for study. The patient was unmarried, American born, and a professional proofreader for many years. Her chief complaints were long-standing unproductive cough, and occasional epigastric distress, accompanied by mild nausea. There is no record of the presence of chest pain, dyspnea, cyanosis, expectoration, ankle edema, or weight loss. The past medical history included a hysterectomy fifteen years before. There was no history of tuberculosis, rheumatism, venereal disease, or glandular enlargement. Physical examination revealed mild obesity, blood pressure of 140/95, edentia, and normal body temperature, pulse, and respiratory rate. Hemoglobin was 15.5 gm. per 100 cc., erythrocyte count, 5,010,000, leukocyte count, 8,800, with 75 per cent polymorphonuclears, 21 per cent lymphocytes, 3 per cent monocytes, and 1 per cent eosinophils. On routine blood smear, the red blood cells and platelets appeared normal. Sedimentation rate was 5 mm. in sixty minutes. The blood sugar was 71 mg. and the nonprotein nitrogen 26 mg. The Hinton test was negative. A single urinalysis failed to reveal any abnormality. Kidney function, as expressed by the phenol-sulfonphthalein test was good, 25 per cent of the dye being excreted at the end of fifteen minutes, and 55 per cent at the end of sixty minutes. The basal metabolic rate was minus 5 per cent. Stool examination was negative for blood and mucus. Oral cholecystography, barium meal, and barium enema failed to show abnormality in the gastrointestinal tract.

Examination of the chest (Fig. 1) revealed a sharply defined, pear-shaped mass, 6 cm. in its greatest diameter, lying in the right cardio-

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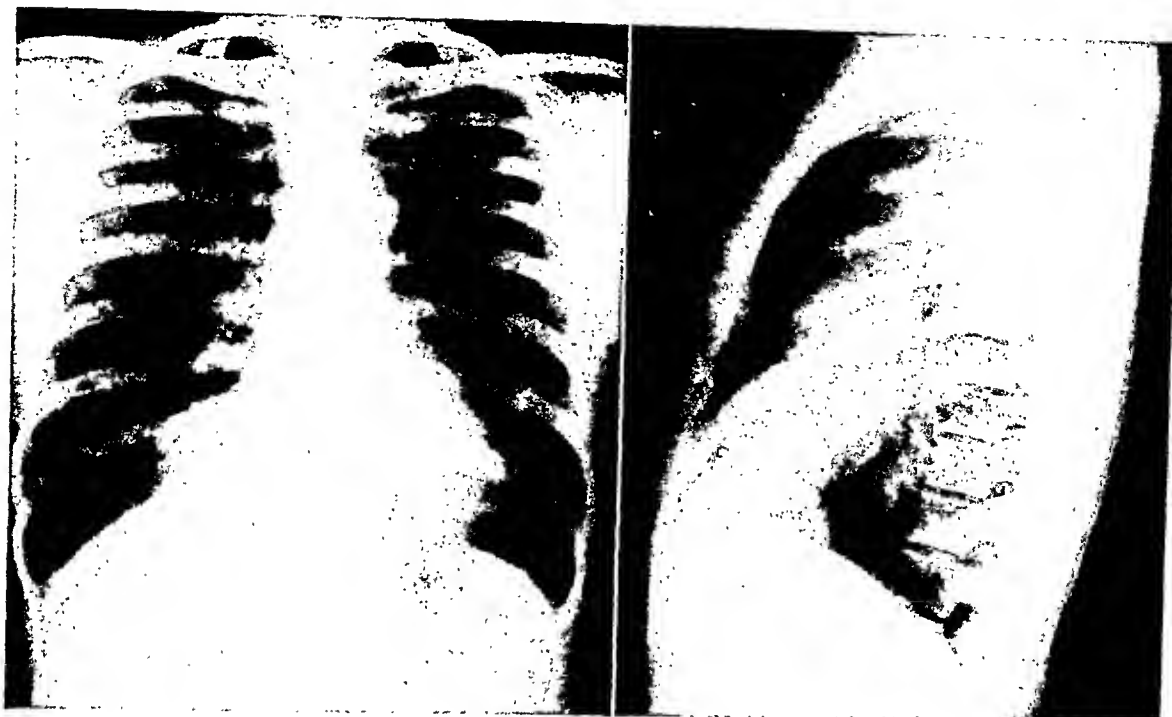


FIG. 1

phrenic angle, against the anterior chest wall. Under the roentgenoscope, the mass moved with the diaphragm; it did not pulsate, nor change size with respiration or change in position. The differential diagnoses considered were fat pad, omental hernia, and mediastinal tumor.

The patient left the hospital untreated, and was observed at intervals by her local physician. She was readmitted to the hospital eleven months later, on December 29, 1942. There had been no increase in the symptoms, and no new ones. Physical examination revealed no change from the findings previously recorded. Roentgenographic examination of the chest showed the mass to be slightly larger than before. On January 2, 1943, the chest was explored.

Operative Findings (Dr. Richard Sweet, surgeon). The chest was opened by an anterior intercostal incision. The tumor was easily found and was obviously cystic in nature. There was no thickening of the wall and no evidence of inflammatory reaction. The only attachment of the mass was to the pericardium. In developing the cleavage plane between the mass and the pericardium, it was noticed that the fluid within the mass began to disappear, and, in squeezing it, all the fluid was expressed into the pericardial cavity. When the pressure was released, the action of the heart slowly pushed the fluid back into the sac, distending

it once more about as much as when it was first seen. This maneuver was repeated several times. The diverticulum was then thoroughly freed, and its communication with the pericardium found. The communicating opening was a little more than 0.5 cm. in diameter. At this point it looked very much like a hernial sac, and the coarse fibers of the pericardium could be seen decussating around the neck of the diverticulum, the wall of which was much thinner than the pericardium. There was no evidence of other disease of the pericardium. The neck of the sac was then opened and the communicating opening actually visualized. The diverticulum was removed and the chest wall closed. The patient had an uneventful convalescence, and was discharged from the hospital on the fourteenth postoperative day.

Pathological Findings. Grossly, the specimen is a roughly retort-shaped sac, measuring 8 by 4 by 1.5 cm. Its external surface is smooth, glistening, thin, and translucent. There was 22 cc. of light yellow, slightly blood-stained fluid in the sac. Microscopically, the lining is composed of well differentiated serosal cells.

DIFFERENTIAL DIAGNOSIS

True pericardial diverticulum is included in the group of diseases presenting themselves as a mass seen in, on, or close to the

heart. These include marked enlargement of one or more chambers of the heart, especially of the left atrium; aneurysm of the heart; tumor of the heart, pericardium, mediastinum, or adjacent lung, especially mediastinal dermoid or benign pericardial adenoma; encapsulated pericardial effusion; aneurysm of the root of the aorta; diaphragmatic hernia close to the heart, and fat pad.

The absence of clinical findings of cardiovascular disease will rule out marked enlargement of one or more of the chambers of the heart, cardiac aneurysm and encapsulated pericardial effusion. Aneurysm of the root of the aorta may be ruled out by absence of other evidence of cardiovascular syphilis, negative serology, and the roentgenological appearance of the rest of the aorta. Barium studies of the gastrointestinal tract will sometimes eliminate the presence of diaphragmatic hernia, depending on what is in the hernial sac. The history, the absence of physical signs in the chest, and possibly lipiodol bronchography will rule out lung tumor.

Differentiation from cardiac, pericardiac, or mediastinal tumor, especially dermoid or benign pericardial adenoma, and from fat pad appears more difficult. Location of the lesion is not especially helpful. The theory of Haas³ as to the sites of predilection, mentioned previously, is confirmed by the fact that the majority of pericardial diverticula occur at the lower right border of the heart, anteriorly, a smaller number higher up on the right border and a smaller number near the location of the left atrium on the left.

Jansson⁴ has found a very helpful sign: in

his case, there was marked change in the shape of the mass in deep inspiration and forced expiration. In inspiration, the mass became long and narrow; in expiration, rounder, shorter, and broader. No such change was observed in our case; however, the diverticulum described by Jansson was four to five times larger than the one described here.

Dr. George W. Holmes⁵ has suggested an interesting possibility in the differential diagnosis; that is, observation in the lateral decubitus position, with the mass higher than the heart, may show diminution in the size of the mass, since the fluid may run back into the pericardial sac, as observed at the time of operation in this case.

SUMMARY

A distinction has been offered between inflammatory sacculation of the pericardium, occurring in the pathogenesis of pericarditis, and true non-inflammatory diverticulum of the pericardium. A case of the latter type is reported.

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RICKETS AND INFANTILE SCURVY OCCURRING IN A CASE OF OSTEOGENESIS IMPERFECTA*

By RALPH S. BROMER, M.D.

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AFFECTIONS of the skeleton may occur simultaneously in children. Examples of this are the combination of rickets and infantile scurvy, congenital syphilis and infantile scurvy, and rickets and lead poisoning.¹ Of these, the occurrence of rickets and scurvy is not infrequent, the development of rickets in a case of congenital syphilis is probably less frequent and the combination of lead poisoning and rickets is rare. A patient was admitted to the Children's Hospital who presented evidence of osteogenesis imperfecta with pathological fractures. At the age of three months he developed rickets and at the age of one year and nine months he was admitted with unmistakable evidence of infantile scurvy.

CASE REPORT†

The patient was a Negro male infant, aged three months, admitted for the first time on

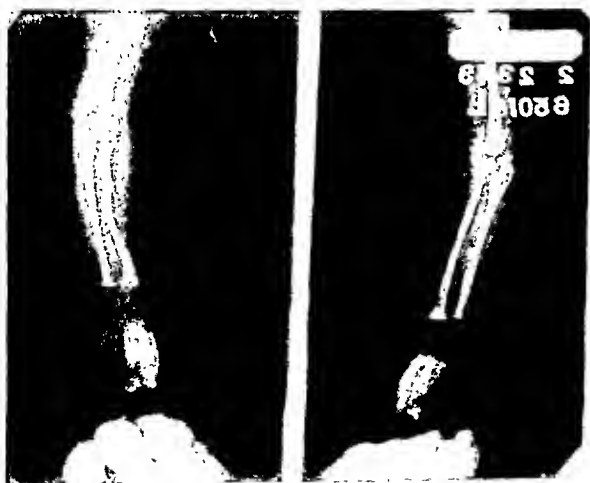


FIG. 1. Note the deformity of the right radius with decalcification and an osteoid zone at the distal end of the diaphysis. Slight flaring of the distal extremity, right radius. Examination made on first admission of patient to the hospital.

† I wish to express my thanks and appreciation to Dr. Joseph Stokes for permission to report this case from his service.

February 19, 1943. The baby was born at full term with an easy labor and a spontaneous delivery. His birth weight was 6 pounds. At two months of age his mother noticed that his head was soft. He had been breast fed for one month and then was given evaporated milk, 8 oz. with two tablespoonsful of karo and water, 13 oz. The mother claimed that orange juice was started at two months and had been given faithfully. He also received, starting at two months, $\frac{1}{2}$ teaspoonful of cod liver oil, daily.

The infant was underdeveloped and undernourished but did not appear to be acutely ill. The head had a soft consistency suggesting a craniotabes. The circumference of the head was $13\frac{3}{4}$ inches, the anterior fontanelle measured $1\frac{1}{4}$ by $\frac{1}{4}$ inches, the posterior fontanelle $\frac{1}{2}$ by $\frac{1}{2}$ inch. The fontanelles were not bulging. On this first admission no bluish tinge of the scleras was noted. In the chest there was a slight prominence of the costochondral junctions. The heart and lungs were normal.

The Wassermann and Kahn reactions were negative. On admission, the serum calcium was 9.2 mg., serum phosphorus was 3.8 mg., phosphatase 17.9 Bodansky units. The blood urea nitrogen was 11.5 mg. By April 23, 1945, the serum phosphatase had dropped to 14.8 Bodansky units.

On admission, the roentgen examination revealed thinning of the cortex of all the long bones. In the forearms decalcification of each radius and ulna was shown, the bones having a slightly streaked appearance. The right radius was curved and deformed which could have been due to old fracture, possibly intrauterine. The distal ends of both bones of each forearm showed spreading, especially the right. The distal end of the diaphysis of the right radius was cupped with a layer of osteoid bone at its extremity, and there was fraying out of the zone of temporary calcification.

In the thorax there was marked atrophy and thinning of the ribs with spreading and cupping of their anterior ends. A fracture of the right clavicle was present with callus formation. Each humerus also was atrophied.

* From the Department of Roentgenology of the Children's Hospital, Philadelphia, Pennsylvania.

In the skull the tables were extremely thin with an open anterior fontanelle and somewhat widened sutures.

At the time of discharge, after treatment with high dosage of vitamin D and calcium chloride, the infant had gained weight and was much improved. The roentgen examination showed an improvement in the degree of calcification of the bones of the forearms, increased density of the zones of temporary calcification and a disappearance of the osteoid zone at the



FIG. 2. Marked thinning and atrophy of the ribs with flaring of their anterior ends. Old fracture of the right clavicle. First admission.

distal end of the diaphysis of the right radius. The patient was discharged on April 30, 1943.

The patient was admitted the second time on August 28, 1944, with a history of illness since August 1, 1944. He was extremely fretful and cried when handled. He lay with both legs drawn up in a frog position. For three days before admission his mother had noticed blood in the stools. She gave a history of adequate feeding except that the child took no orange juice. The patient's weight was 14 pounds. On physical examination he appeared to be acutely ill, was malnourished and underdeveloped. The head gave the impression of possible cranio-



FIG. 3. Marked thinning of all bones of the vault of the skull with lack of normal calcification persisting after seven weeks of antirachitic therapy.

tabes. A slight bluish tinge was noted in the scleras. The gums were sore and bleeding. In the chest there were enlarged costochondral junctions but no Harrison's groove. All joints were tender and enlarged.

On August 29, serum calcium was 9.4 mg. and phosphorus was 4.1 mg., phosphatase was 6.8 Bodansky units.

On roentgen examination the long bones showed extreme thinning of the cortex, and atrophy more marked than on the first examination. The atrophy was especially prominent in each fibula. Typical scorbutic hemorrhages



FIG. 4. Increased calcification of the diaphyses of the bones of the forearms with disappearance of the osteoid zone at the distal end of the right radius, after seven weeks of antirachitic therapy.

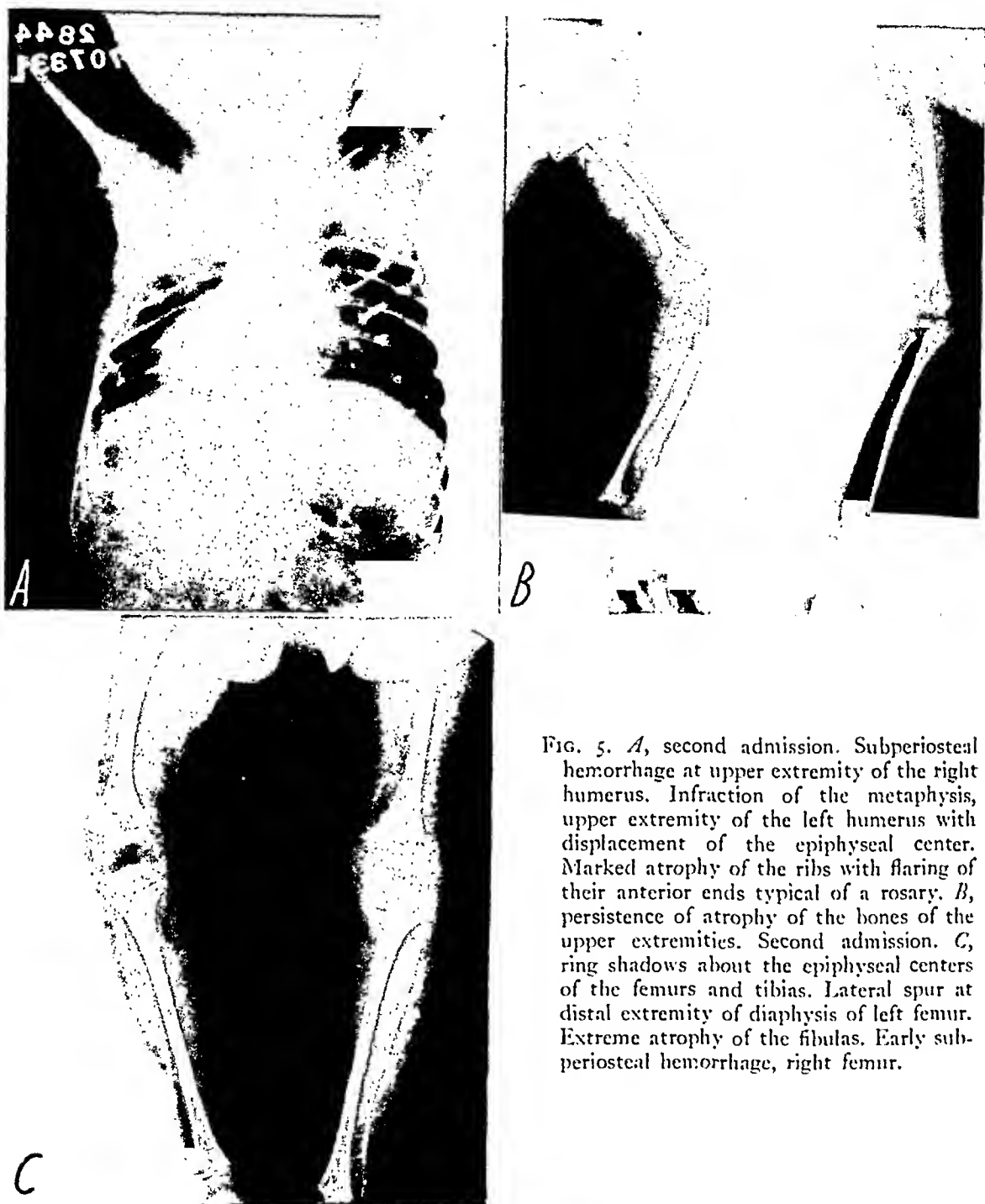


FIG. 5. *A*, second admission. Subperiosteal hemorrhage at upper extremity of the right humerus. Infraction of the metaphysis, upper extremity of the left humerus with displacement of the epiphyseal center. Marked atrophy of the ribs with flaring of their anterior ends typical of a rosary. *B*, persistence of atrophy of the bones of the upper extremities. Second admission. *C*, ring shadows about the epiphyseal centers of the femurs and tibias. Lateral spur at distal extremity of diaphysis of left femur. Extreme atrophy of the fibulas. Early subperiosteal hemorrhage, right femur.

were present in the upper end of the diaphysis of the right humerus and in the distal end of the diaphysis of each femur. In the upper end of the diaphysis of the left humerus there was a metaphyseal infraction with displacement of the epiphyseal center. Distinct ring shadows were visible in the epiphyseal centers of the upper ends of the tibias and the lower ends of the femurs.

In the thorax marked spreading and cupping of the anterior rib ends with extreme thinning and atrophy were present. The appearance was that of a rosary, most likely of scorbutic origin. The old fracture of the right clavicle was still visible.

The tables of the skull were better calcified than on the first admission but they were still somewhat thinner than normal. A mosaic ap-



FIG. 6. *A*, subperiosteal hemorrhages in the distal ends of the diaphyses of the femurs, one month after antiscorbutic treatment was started. *B*, appearance of the skull, one month after second admission (age, twenty-two months). Note thinning of the tables with mosaic appearance of the occipital area.

pearance, due to large wormian bones in the occipital and posterior parietal areas had developed since the last examination. The sutures were again wider than normal.

The child was placed on a high caloric diet and was given therapeutic doses of all vitamins. On discharge his legs were fairly well extended and roentgen examination showed satisfactory healing of the scorbutic hemorrhages. His gain in weight was not, however, satisfactory and he had only gained 1 pound when discharged on November 11, 1944.

He was admitted for the third time on November 11, 1944. He had fallen from a highchair the day previous to admission. He held his left leg immobile. His mother stated that she had put him to bed immediately after the fall where he remained without complaint. The roentgen examination showed a fracture of the left femur in the distal third with some bowing of the fragments, convexity anterior. The rings about the epiphyseal centers of the femur and tibia had become denser and wider and there was increased calcium deposition in the cortex of the shafts. Atrophy was still present, especially in the fibula. He was discharged on December 13, 1944. The bluish tinge of the scleras was again noted on this admission.

On February 4, 1945, he was admitted for the fourth time. There was no history of a definite trauma. On roentgen examination a fracture of the right humerus was found located at approximately the junction of the upper and middle thirds of the bone. He had been in good con-



FIG. 7. Well developed subperiosteal hemorrhage in healing stage, upper end of the right humerus after six weeks of antiscorbutic treatment during second admission. Note healing of the infraction in upper metaphysis of the left humerus.



FIG. 8. Third admission. Fracture of the left femur in the distal third. Increased density and width of the rings about the epiphyseal centers and of the zones of temporary calcification.

dition from the date of his previous discharge until three days before admission when he developed a severe cough and had refused to eat. His mother brought him to the hospital because of this and not because of any symptoms referable to the fracture. On both the third and fourth admissions he had a chronic otitis media. He was discharged on March 14, 1945.

DISCUSSION

Osteogenesis imperfecta tarda is characterized roentgenologically by the typical gnarled appearance of the bones of the extremities with marked deformities caused by the multiple fractures. The cortex is thin. Callus deposits can be detected in the shafts at the sites of the fractures. The thorax is compressed and the ribs are bent. The bones usually show a marked degree of osteoporosis. The tables of the skull are extremely thin and often calcification and ossification seem to be entirely lacking in some areas. Sutures are wide.

Clinically the skull on pressure is no thicker than parchment due to defective membranous bone development. This has

led to the term "rubber ball head." Knaggs⁶ called attention to the fact that the membranous areas which intervene between the immature bone are apt to become filled with numerous wormian bones resulting from discrete patches of ossification. The vault is thus represented by a mosaic of larger and smaller bone plates, sometimes touching one another and sometimes united by bridges of periosteum and dura. In some cases, the skull can be moulded by pressure of the hands.

Osteogenesis imperfecta tarda is characterized in the roentgenogram by marked thinning of the cortex of the long bones and deformity usually dependent upon the number of fractures present. There may, however, be bowing without actual fracture. Generalized osteoporosis may be seen. The metaphyses and epiphyses have a



FIG. 9. Fourth admission. Fracture of the right humerus. Persistence of atrophy of shafts.

widened appearance for the most part due to the atrophy of the shafts. The area of the diaphyso-epiphyseal junction is usually normal. Slight infractions of the periosteum may be seen sometimes rather than actual fracture. In such areas callus formation can later be found. There is often a noticeable lack of pain accompanying the fractures. This has been accounted for by the subperiosteal nature of many of the fractures. Knaggs believes that, in the cases in which signs first appear in childhood or adolescence, the fundamental change was present in early uterine life. The less the defect, the greater is the likelihood that its signs will be delayed until the patient is able to get about and is exposed to the ordinary slight traumatism of a usually healthy life. As a rule, the earlier in life the fractures first occur, the greater is the liability to fracture.

The diagnosis of osteogenesis imperfecta can be justified by the following: the occurrence of multiple fractures, some without history of trauma; the roentgen appearance of extreme atrophy of the shafts of the long bones and ribs and the apparent widening of the epiphyseal and diaphyseal areas; the lack of pain accompanying the fractures; the bluish tinge of the scleras. No history of occurrence in other members of the family could be obtained but this absence of a familial or hereditary tendency does not rule out the diagnosis as the non-hereditary occurrence of osteogenesis imperfecta or osteopsathyrosis has been reported quite frequently in the literature. Such cases have been included in a separate category in the classification of the disease by Key.⁵

The presence of the fracture of the right clavicle and the deformity of the right radius suggests that the condition was present at birth and during intrauterine life. The roentgen appearance is not that of the usual type of osteogenesis imperfecta congenita but is more like that of the late types. The unusual feature is the presence of this roentgen appearance in early infancy with some evidence that it was present at birth. Foote³ has described an infant

tile type that appears after the child begins to walk or stand without support. These children usually die comparatively early as a result of intercurrent infection.

The signs indicative of rickets on the first admission of the patient are as follows: decalcification of the bones of the forearms and lower extremities; the fraying out of the zones of temporary calcification in the distal end of the right radius with the presence of an osteoid zone; the tendency to widening and spreading of the diaphyseal ends and the similar appearance in the rib ends due to enlargement of the costochondral junctions.

The craniotables of the skull could be due either to rickets or to osteogenesis imperfecta. Park and Eliot⁷ state that the craniotables of osteogenesis imperfecta is fully developed at birth, is far more extensive than in rickets and involves the anterior half of the skull as well as the posterior half. In osteogenesis imperfecta there are sometimes scattered islands of bone. They also call attention to the fact that in normal infants, one or two months old, but more frequently in premature babies, thinness of the skull may be found which is of no pathological significance. In the skull of the case reported here there was only a uniform thinning of the tables with lack of calcification. On the second admission a mosaic appearance had developed which suggests involvement due to osteogenesis imperfecta. It would seem logical to assume that the rickets was of mild degree and that the condition of the skull was not due solely to rickets. However, increased calcification and slight thickening of the tables occurred after antirachitic treatment was begun.

The occurrence of subperiosteal hemorrhages confirms the diagnosis of infantile scurvy. In addition, there were definite ring shadows about the epiphyseal centers. Other signs such as thinning of the cortex, the ground glass appearance of the metaphyseal areas extending toward the middle of the shafts and the zone of rarefaction adjacent to the zone of temporary calcification, were obscured by the markedly

atrophic condition of the bones present from birth. The spreading and cupping of the rib ends due to marked enlargement of the costochondral junction found on the second admission could have been due to a scorbutic rosary.

Czerny and Keller² drew attention to multiple fractures with general fragility of the bones occurring in infants which they ascribed to a special form of avitaminosis and which they believed should not be included in the category of osteogenesis imperfecta of either the congenital or late types. This was later emphasized by Heise⁴ who suggested that as blue sclera is an indication of originally weakened mesenchyme, the patients are less resistant to bone diseases in general. He reported the cases of two children, twins, who after attacks of scurvy showed fragility of the bones with fractures. He felt that they could not be considered as cases of fragility due to osteogenesis imperfecta but of fragility due to avitaminosis. The fact that fractures were present before the occurrence of the scurvy would rule out such cause in the patient under consideration.

SUMMARY

A case is reported of a male Negro infant

who showed evidence of osteogenesis imperfecta apparently present from birth. Rickets developed at the age of three months and infantile scurvy at twenty-one months. The unusual feature of the case is the presence at an early age of osteogenesis imperfecta with some evidence that it was present from birth and that the type of roentgen changes in the skeleton was indicative of the late type of the disease rather than the congenital.

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GENERALIZED LEONTIASIS OSSEA*

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L EONTIASIS OSSEA is an uncommon disease, consisting of diffuse bony thickening, usually confined to the skull (notably the bones of the face) but occasionally associated with involvement of the long bones. It is also known as hyperostosis of the skull, megalcephaly, fibromatosis osteoplastica ossium and hyperostose des os de la tête. The condition was first described by Malpighi in 1697 but was not called leontiasis ossea until 1864 when Virchow described it in considerable detail. It is said that the name was chosen because the bony overgrowth corresponded with the overgrowth of connective tissue seen in mollusum fibrosum with leonine facies.³ The hyperostosis may be limited to one bone of the skull or involve all of them; in the latter event, the bones of the face may be much enlarged and distorted, but the facies, despite the name, is almost *never* leonine. Skulls of considerable thickness (calvarium of 5 cm.), and weight (4,000 gm.) have been reported.

The disease begins in childhood or adolescence. Females are said to be more commonly afflicted than males.

The cause of the disorder is unknown. Infectious, metabolic and endocrine origins have been postulated but none proved. Because some cases, both grossly and microscopically, have resembled cases of osteodystrophia fibrosa hyperostotica (Paget's disease), the condition has been erroneously regarded as a cranial form of osteitis deformans.

PATHOLOGY

The process may involve one or all the bones of the skull, and sometimes, the long bones. Grossly, Knaggs⁶ divided it into two types, the creeping periostitic and the diffuse osteitic type. The histopathological changes are the same in both, but subperiosteal bony deposits are larger in the

periosteal type. The following pathological description is given by Bauer:¹

Early in the disease one notes disappearance of the usual bony structures. The outer layers are less compact, and areas of bone dissolution appear filled with vascular and fibrous connective tissue which may subsequently become fibrosed. New bone may be laid down in irregular fashion in such fibrous areas, although neither the laminations nor the haversian systems of normal bone are formed. Small cysts may remain. In the later stages, the bone loses its normal contour and is greatly thickened and porous. When suppuration is present, it is the result of secondary infection. Isolated bone sections may resemble either Paget's disease or osteitis fibrosa cystica except that the fibrosis is more marked in leontiasis ossea.

SYMPTOMS

The symptoms vary widely, for no obvious reason. Some cases, with slight involvement of the skull, allege that they suffer marked headache and various visual or auditory disturbances; others, with extensive hyperostosis, are virtually asymptomatic. The overgrowth of the malar or mandibular bones produces facial deformity which may disturb the patient more or less in proportion to his amour propre.

Headache is sometimes a severe symptom. Exophthalmos is frequently present. Visual and hearing defects, neuralgia, and nasal and lacrimal duct obstruction have been reported. Insomnia, mental dullness and convulsions may develop. The course of the disease is quite variable (from twenty to forty years). Death has been reported from cachexia and from convulsions.³

DIAGNOSIS

The diagnosis is usually made by roentgen examination of the skull, with the finding of diffuse hyperostosis of the bones of the face (notably the malar, frontal and

* The opinions and views set forth in this article are those of the writer and are not to be considered as reflecting those of the Navy Department.

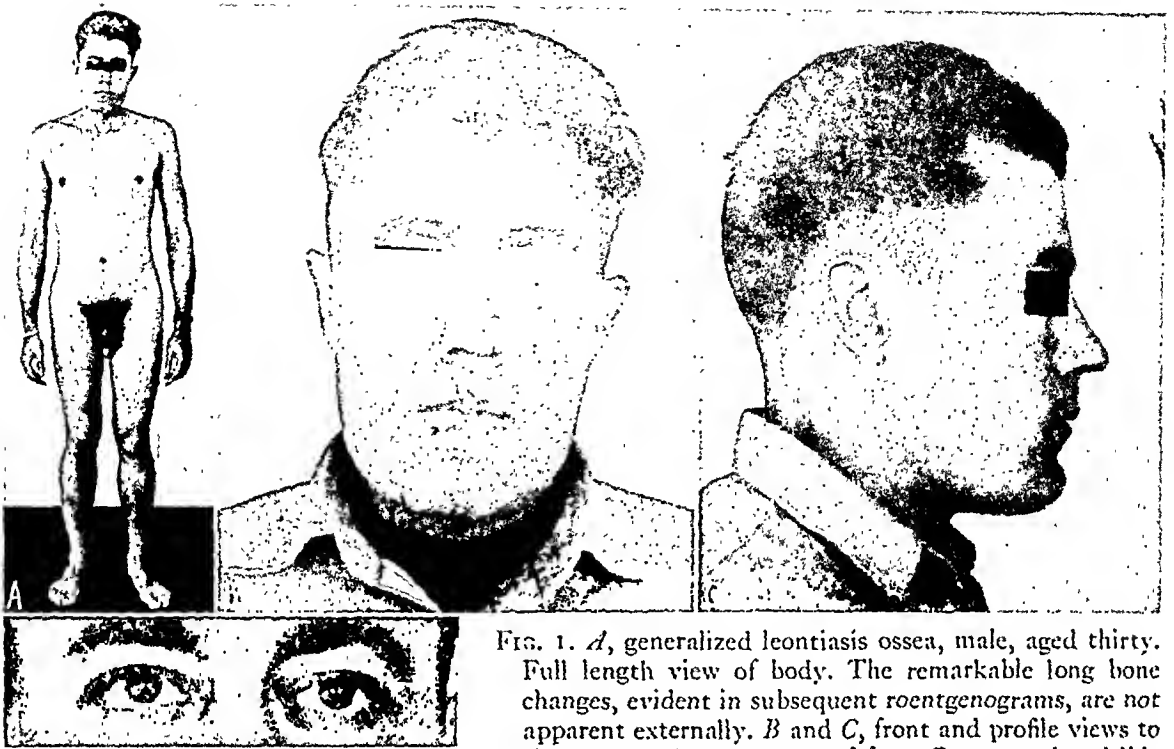


FIG. 1. *A*, generalized leontiasis ossea, male, aged thirty. Full length view of body. The remarkable long bone changes, evident in subsequent roentgenograms, are not apparent externally. *B* and *C*, front and profile views to show external appearance of face. Compare the visible

size of the mandible with that seen in the subsequent roentgenograms. *D*, close up of eyes. The degree of exophthalmos was more apparent than the photograph shows.

sphenoidal bones). There are variable degrees of actual bony overgrowth and occasionally enormous thickening of these bones. The hyperostosis is usually uniform and "osteomatous," and not associated with macroscopic areas of porosis or cystic change. The mandible and any of the other bones of the skull may be involved. Rarely, there is diffuse cortical hyperostosis of the long bones of the extremities, usually bilateral and symmetrical in distribution.

The differential diagnosis includes chronic inflammatory osteitis (pyogenic or syphilitic), Paget's disease and acromegaly. We doubt if chronic radium poisoning or chronic fluorosis would require differentiation. In inflammatory osteitis the involvement is usually not bilateral and symmetrical (as it tends to be in leontiasis ossea) and sequestra may be present. In Paget's disease, the characteristic nummular areas of porosis and sclerosis, plus the diffuse striated nature of the hyperostosis, will usually serve to distinguish the entities. Further, in the latter, the pelvis, spine or long bones will frequently

show characteristic changes that help to identify the process. Leontiasis ossea tends to appear in younger age groups, Paget's disease in older persons. In acromegaly the jaw bone is mainly elongated and hypertrophied, not grossly hyperostotic or osteomatous; the sella turcica may be enlarged; the hands will show characteristic growth changes, both soft tissue and phalangeal. The entire skeleton may be increased in size.

Inasmuch as leontiasis ossea with involvement of the long bones is a rare clinical entity, it is deemed worth while to place the following case on record.

CASE REPORT

The patient was a white male, aged thirty, a machinist's mate in a Construction Battalion. He first sought medical attention on account of intermittent frontal headaches and progressive enlargement of the jaw.

Present Illness. At first, he stated that his headaches and jaw changes were only of one year's duration (he had enlisted about fourteen months prior to his visit to sick bay); however, on further questioning, he admitted



FIG. 2. Generalized leontiasis ossea. *A*, frontal; *B*, dorsal; *C*, lateral, and *D*, Waters projection of the skull. Note the hyperostotic changes in the frontal, sphenoidal, and temporal bones; the petrous apices show dense sclerosis; the upper portions of the parietal bones and the central portion of the occipital bone show moderate hyperostosis.

he had had headaches for a period of about five years, especially on stooping over, and that his jaw had begun enlarging about two and

one-half years ago. His eyes had been more prominent than usual for a similar period, and the hearing in his left ear had been getting

slowly worse during that time. He had concealed these symptoms at time of enlistment, being then anxious to escape from some domestic difficulties. His bilateral exophthalmos had been noted at time of induction, but not his prognathism.

Previous History. Aside from that noted under present illness, this was not remarkable. He had no childhood diseases or injuries of

feet, 10 inches; weight 160 pounds. Exophthalmos, bilateral, of a fairly marked degree, but without lid lag (Fig. 1D). Vision in both eyes 20/15. Ocular fundi negative. Visual fields and acuity normal. Ears externally negative; audiograms revealed slight impairment of hearing in left ear; right ear normal. Marked symmetrical enlargement of the mandible, not quite so pronounced at the symphysis as elsewhere.

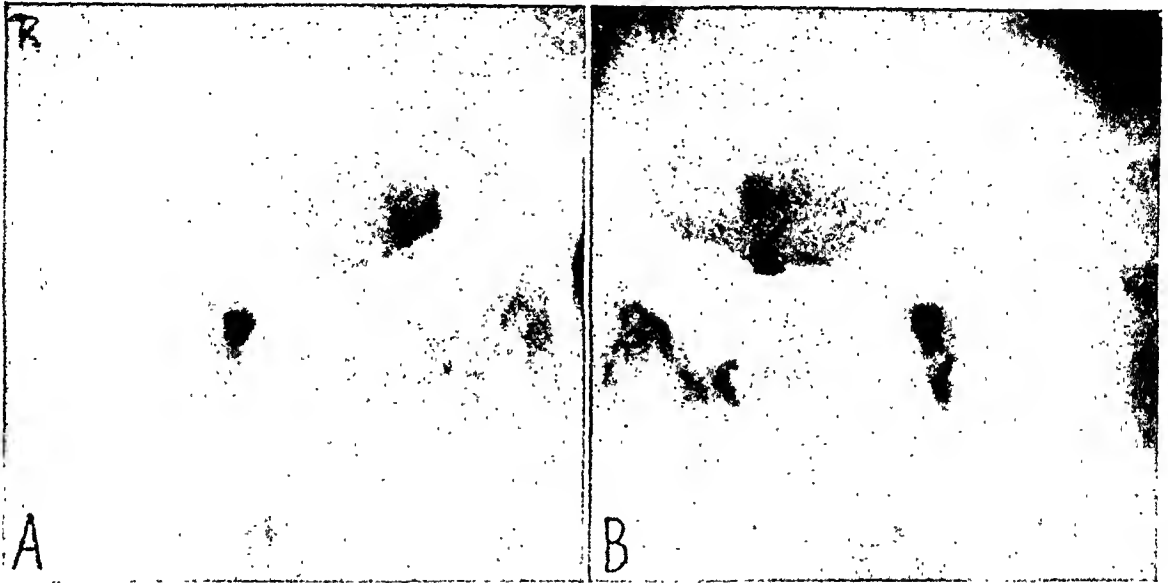


FIG. 3, A and B. Optic foramina. The optic foramina are slightly smaller than average (direct measurement on 36 inch target film distance roentgenograms being: left, 3.5×5 mm.; right, 3.5×4 mm.).

note; no history of lues. He was born in Nebraska. He had worked as a farm hand in his youth and in construction jobs since that time.

Family History. His father and mother died when he was an infant, of causes unknown. Both were natives of Nebraska; neither had enlargement of the jaws or other bones, as far as he was aware. He has one brother, aged thirty-nine, with "such extensive enlargement of the jaw that he was rejected for military service"; this brother was told "by an Omaha clinic that he had an incurable bone disease, and is being treated for acromegaly." The patient is married and has two children, living and well, without bony deformities.

Physical Examination. A well developed male, with a slightly prominent jaw, in no apparent distress (Fig. 1, A, B, C). Height 5

No tenderness, nor limitation of motion of the jaw. Remaining bones of face, grossly negative. Reflexes negative. Temperature 98.6°F ., pulse 88, respiration 22, blood pressure 120/70.

Laboratory Examinations. Red blood cells 4,140,000 per cu. mm. White blood cells 9,200 (65 per cent neutrophils; 36 per cent lymphocytes). Sedimentation rate normal. Hemoglobin 14 gm. Blood calcium 10 mg. per 100 cc. Blood phosphatase studies not available. Kahn reaction negative. Urinalysis negative.

Roentgen Examination. Skull: There is diffuse and remarkable hyperostosis of the inferior half of the frontal bone, involving notably the orbital ridges and the floor of the anterior fossa; similar changes are present in the sphenoidal bone, the mandible, and portions of the malar and temporal bones (Fig. 2, A, B, C, D). There is slight generalized hyperostosis of por-



FIG. 4. *A*, left humerus; *B*, radius and ulna; *C*, wrist and hand. Similar changes were present in the right arm and hand. Note the diffuse thickening of the cortex of the humerus. The changes in radius and ulna resemble extreme osteoperiostitis. The hyperostosis of the shaft of the right second metacarpal was more marked than that of the left; otherwise the changes in the hands were identical.

tions of the remainder of the calvarium, especially at the vertex and about the external occipital protuberance. The diploe is virtually obliterated. The optic foramina appear to be a trifle narrowed (direct measurements on 36 inch target film distance roentgenograms being left 3.5×5 mm. and right 3.5×4 mm.) (Fig. 3, *A* and *B*). The auditory canals are not visibly narrowed, but portions of the temporal bones show the above mentioned hyperostosis.

Spine, Ribs, Sternum and Pelvis: Roentgen appearance normal (Fig. 5).

Chest: Heart vessel shadow negative; transverse cardiac diameter 12 cm. Healed primary complex in middle third of left lung. Lungs otherwise clear.

Kidney, Ureter, Bladder: Normal. No renal opacities.

Upper Extremities: Diffuse thickening of the cortex of each humerus, with virtual obliteration of the cancellous spaces in the distal half of each bone. The cortex reaches 23 mm. in thickness in certain areas. Diffuse hyperostosis, somewhat resembling the so-called "flowing" type, involving the proximal third of each ulna and the middle three-fourths of each radius. The appearance here is one of extreme osteoperiostitis. There is hyperostosis of the shafts of the second and third metacarpals of each

hand (more marked on the right side) without evidence of involvement of the other bones of the hands at the present time (Fig. 4, *A*, *B*, *C*).

Lower Extremities: Diffuse thickening of cortex of the shaft of each femur, and of the shaft of each tibia and fibula. In places, notably on the tibiae, the appearance is one of "creeping periostitis." The cortex of each tibia shows major changes on its mesial, lateral and posterior aspect (not on its ventral) (Fig. 6, *A*, *B*, *C*). There is no patchy porosis or other

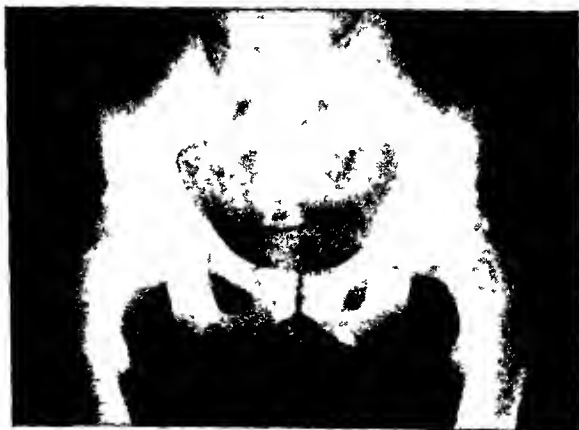


FIG. 5. The pelvic bones are not involved. Neither were the ribs, clavicles, sternum, nor vertebrae.

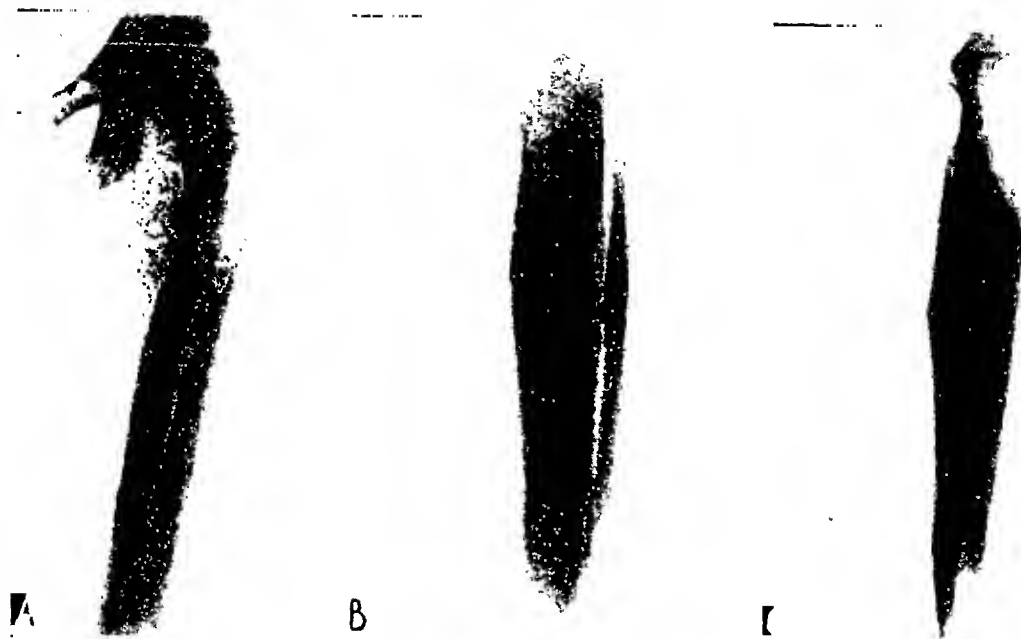


FIG. 6. *A*, left femur; *B*, tibia; and *C*, fibula. Similar changes were present in the right leg. The femoral thickening is essentially a diffuse cortical hyperostosis. The tibial changes are most marked on the dorsal, mesial and lateral aspects of the bone (in contradistinction to the usual location of the changes in Paget's disease). They are pseudo-inflammatory in appearance. The feet showed no bone changes.

evidence of Paget's fibrous dystrophy. Both feet are negative.

Conclusion: Generalized hyperostosis of portions of the skull and the bones of the extremities (generalized leontiasis ossea). The resemblance of the changes in the calvarium to those of Paget's disease and the slight resemblance of the changes in the arm bones to those of melorheostosis Léri is noteworthy, but we believe the basic lesion to be an unusual type of leontiasis ossea.

DISCUSSION

This case is of considerable interest for several reasons: (1) the virtual absence of involvement of the maxillae, (2) the extensive involvement of the bones of all four extremities and, especially (3) the fact that *both* of Knaggs' "types" of leontiasis ossea are present in one and the same patient, the osteitic (as shown best in the mandibular and femoral changes) and the periostitic (evident in the radial and tibial changes).

There is a surprising amount of confusion between Paget's disease, acromegaly and leontiasis ossea in the literature, even in authoritative textbooks.^{2,4,5,7} In Ewing's

"Neoplastic Diseases"⁴ appears the sentence: "In acromegaly there is diffuse overgrowth of the bones of the skull and extremities, resulting from disturbance of hypophyseal function (leontiasis ossea)."

In Boyd's "Pathology"² we find the statement: "In Paget's disease the bones of the face are occasionally greatly thickened (leontiasis ossea)." MacCallum's "Textbook of Pathology"⁷ carries an identical sentence.

In the introduction to "Roentgen Interpretation" by Holmes and Ruggles,⁵ it is stated that in leontiasis ossea the mandible is *not* usually involved: "Leontiasis ossea or creeping periostitis is somewhat similar to hyperostosis frontalis. It may spread slowly over the maxillae, frontal and parietal regions. Usually, the mandible is not involved. The condition may be confused with Paget's disease."

We believe that the case under review is one of idiopathic (perhaps congenital) overgrowth of the cortical portions of many of the bones of the skull and extremities, and fits into the classification of generalized leontiasis ossea. Saucerotte¹

is said to have reported such a case, but details thereof are not presently available to the writer. The type of hyperostosis, the absence of porotic changes and the anatomic distribution all favor the diagnosis given. If only a few of the involved areas of the skeleton had been examined, it might have been classified as the creeping periostitic type of Knaggs, while, if others were roentgenographed, it might have been classified as the diffuse osteitic type.

The prognosis of cases such as the one reported herewith is obviously poor. Should the exophthalmos be progressive, surgical decompression of the orbital cavities will presumably be necessary. Plastic procedures on the mandible are conceivable, though of dubious utility. Progressive hyperostosis of the long bones with obliteration of the marrow spaces will probably result in some degree of anemia. Continued changes in the temporal bones may result in further impairment of hearing.

SUMMARY

1. Leontiasis ossea is a rare but definite clinical entity, apparently not related to Paget's disease, acromegaly or other conditions sometimes associated with facial bone enlargement.

2. Leontiasis ossea is usually confined to the bones of the face and skull, but a small number of cases also show diffuse and remarkable cortical hyperostotic changes in the long bones of the extremities (generalized leontiasis ossea).

3. A case of generalized leontiasis ossea in a male aged thirty years is reported. The cranial bones and mandible showed typical diffuse "osteitic" overgrowth; the long bones of the extremities showed diffuse, symmetrical cortical and periosteal overgrowth.

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THE HISTOLOGIC EFFECTS OF RADIOPHOSPHORUS ON NORMAL AND LYMPHOMATOUS MICE*†

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IN EARLIER papers^{11,12} the distribution of radiophosphorus (P^{32}) in normal and lymphomatous§ mice has been described. In addition, its effect on the normal blood forming tissues has been observed.^{1,14} On the basis of these investigations P^{32} has been applied therapeutically in the treatment of chronic leukemia.^{2,4,7,8,9,13,15} To gain further knowledge of the radiation effects of P^{32} we have used a transmissible lymphoma in mice.

PART I

Histologic and Hematologic Effects of P^{32} .

Two series of experiments were performed on normal and lymphomatous mice as follows: In Series I, two groups of "A" strain mice (aged five months, sexes mixed) were used. In the first group of 13 mice, 7 received an intravenous injection of approximately 1.2×10^7 lymphoma cells.¹⁰ The other 6 mice were used as controls. Of the 14 mice in the second group, 8 received a similar dose of lymphoma cells, and the 6 remaining mice acted as controls. (The age of this second group of mice was three months, and the sexes were mixed.)

Thirteen days after inoculation, 3 leukemic animals in each group were given 1.0 cc. of an isotonic solution of sodium phosphate intravenously which contained 195.3 microcuries|| of P^{32} per c.c. Five control animals received a similar dose of P^{32} at the same time.

In Series II, 12 mice (three month old

males) were given 1.2×10^7 lymphoma cells intravenously, and seven days later half of these animals received four 1.0 cc. subcutaneous injections (54.5 microcuries per cc.) at two hour intervals. Four normal animals received similar P^{32} injections and 2 additional mice were kept as controls.

Blood Studies. Cells with ring (doughnut) shaped nuclei were classified as "early granulocytes"; large lymphocytes with immature nuclei and abundant cytoplasm were classified as "early lymphocytes"; "large lymphocytes" includes monocytes; lymphoma or leukemic cells were identified by their large size, primitive nucleus, scarce and strongly basophilic cytoplasm. The white cell counts taken on the normal mice were subject to wide variation.

The course of the total white counts after P^{32} administration is shown in Figure 1. It will be noted that, in both series, the drop in white cell count in leukemic animals was greater than that in the normal during the first four days after injection with P^{32} . In the following five day interval (four to nine days after P^{32} administration) the drop of the white cells for Series I approached a plateau while the drop in Series II continued, but at a slightly diminished rate. Following this period the leukemic animals of Series I showed an increasing total count while those of Series II continued to decrease.

In Figure 2 is shown the differential effect of P^{32} on the white cells of normal mice. The small lymphocyte was at first the most markedly affected; while the mature granulocyte was comparatively little affected. Four days after P^{32} injection the drop of the lymphocytes reached a

§ When implanted subcutaneously, a local tumor develops followed by leukemic invasion. After intravenous injection of lymphoma cells, no local tumor develops but a leukemic picture is the result.⁴

|| Beta-ray standard.

* This work was supported by the Columbia Fund for Medical Physics of the Columbia Foundation.

† This work was completed in 1940 but it was not possible to report it at that time, due to transference of our activities.

‡ Department of Physics.

plateau, while the granulocytes began to drop at a greater rate. This drop continued at least to the fourteenth day. However, after the ninth day the small lymphocytes showed a slight rise.

Figure 3 shows the effect of P^{32} on the white cells of leukemic mice. They were affected in a manner similar to that ob-

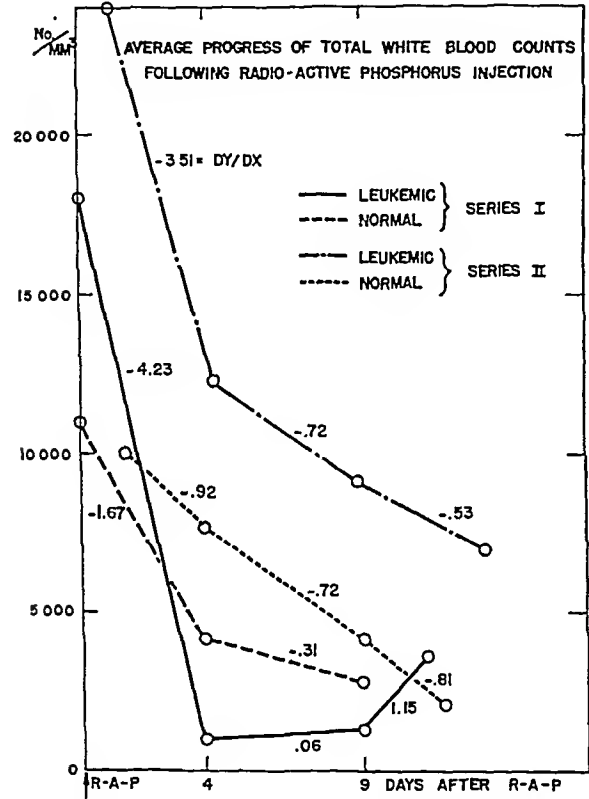


FIG. 1

served in the control animals. In addition, it can be seen that P^{32} was effective in decreasing the number of leukemic cells in the blood for as long as nine days after administration of this particular dose of P^{32} .

Red cell counts and hemoglobin determinations were not carried out, but with these relatively large doses of P^{32} , one would expect after a period of time very low red counts and hemoglobin values.⁸ It should be pointed out that the lethal dose for mice is in the neighborhood of 70 microcuries. The doses used in these hematological and histological experiments

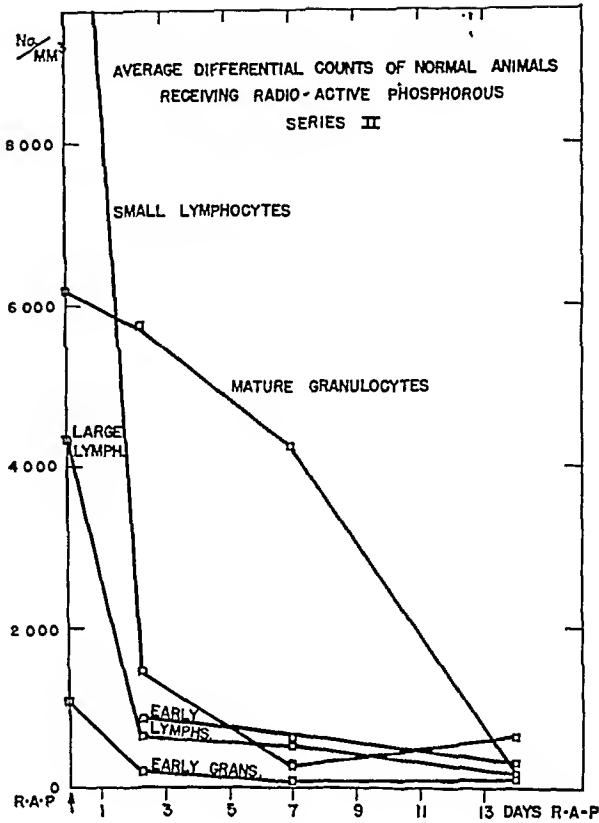


FIG. 2

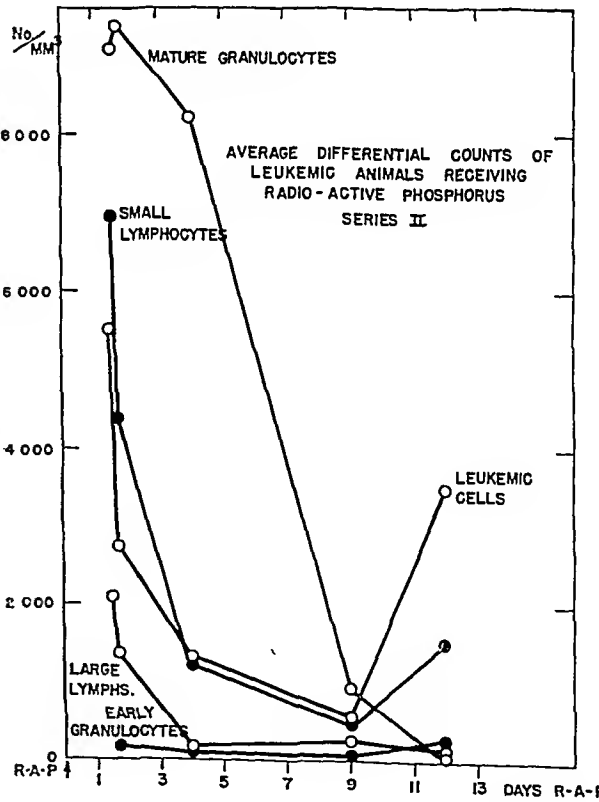


FIG. 3



FIG. 4. Normal mouse bone and marrow. $\times 70$.



FIG. 5. Bone and marrow 214 hours after injection of 218 microcuries of radiophosphorus. Note aplastic appearance. There is a preponderance of mature and nucleated red blood cells. $\times 70$.

have been purposely high in order to bring out the differential effects of P^{32} .

Histologic Studies of Tissues. In the bone marrow of normal mice treated with P^{32} , early granulocytes showed a slight increase sixty hours after P^{32} administration. A decrease followed which persisted for about five hundred hours when a slight increase was again noted. The megalokaryocytes



FIG. 6. Leukemic (twenty days) bone marrow. $\times 70$.

were relatively unaffected. At sixty hours there was no increased vascularization, and at five hundred hours vascularization was decreased. The marrow presented an aplastic appearance, with red blood cells and early red blood cells forming the chief elements (see Fig. 4 and 5).

Eight days after injection with lymphoma cells the marrow appeared normal. As tissue infiltration with these cells progressed, there was a decrease in the number of early white blood cell forms and the megalokaryocytes disappeared. No significant change in vascularity was ob-

served. The lymphoma cells formed a solid mass at twenty days and occupied the entire marrow cavity (see Fig. 6).

When the leukemic mice were given P^{32} eight days after lymphoma injection, many normoblasts were present in the marrow six days after that. The megalokaryocytes remained normal in number and appear-



FIG. 7 Leukemic (twenty days) bone marrow 306 hours after injection of 218 microcuries of radiophosphorus. $\times 70$

ance until they disappeared. The granulocytes increased up to sixteen days after lymphoma injection and then decreased until at twenty days they were practically absent. No marked number of lymphoma cells were noted until twenty days, and even at that time the extent of the invasion was much less than that in the untreated animals (see Fig. 6 and 7).

In the mice receiving lymphoma, slight lymphomatous infiltration occurred in the liver after twelve days. At twenty days substantial perivascular infiltration with these cells was noted. In the terminal stages of the disease the blood vessels of the liver appeared to be dilated. The blood vessels



FIG. 8. Normal mouse liver. $\times 830$.

of the livers of the lymphomatous animals showed definite dilatation eight days after P^{32} injection. No infiltration by lymphoma cells was observed until twenty days after lymphoma transmission. At that time and thereafter, the degree of infiltration appeared to be much less than in those



FIG. 9. Mouse liver 526 hours after injection of 218 microcuries of radiophosphorus. $\times 830$.



FIG. 10. Leukemic (twenty days) liver. $\times 830$.

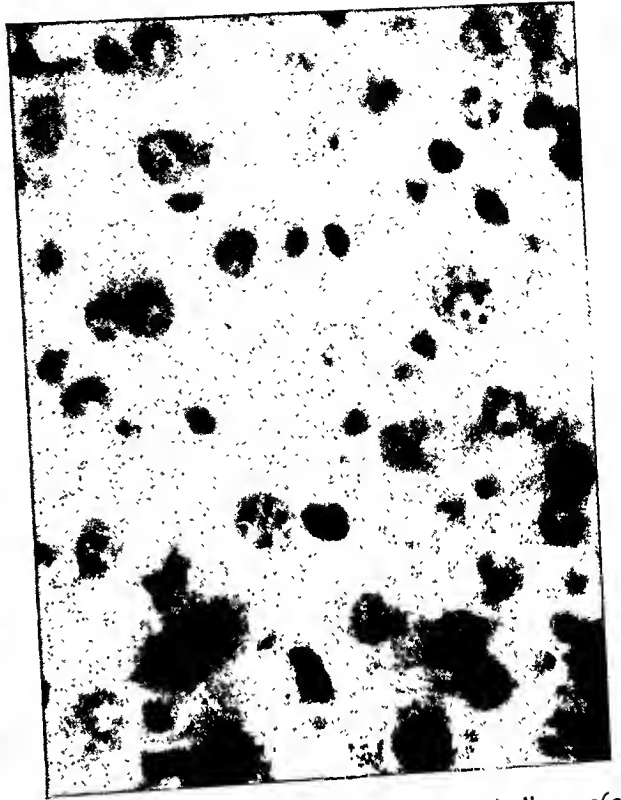


FIG. 11. Leukemic (twenty-two days) liver 360 hours after injection of 318 microcuries of radiophosphorus. $\times 830$.

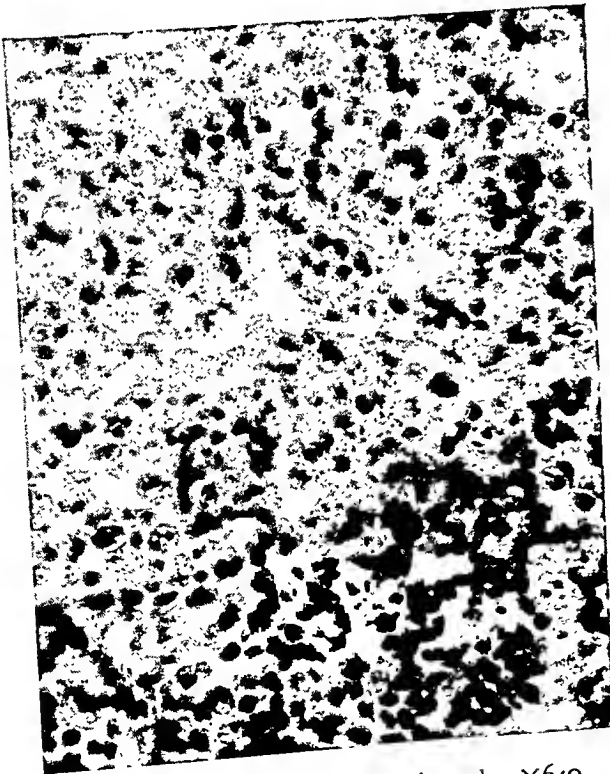


FIG. 12. Normal mouse lymph node. $\times 640$.

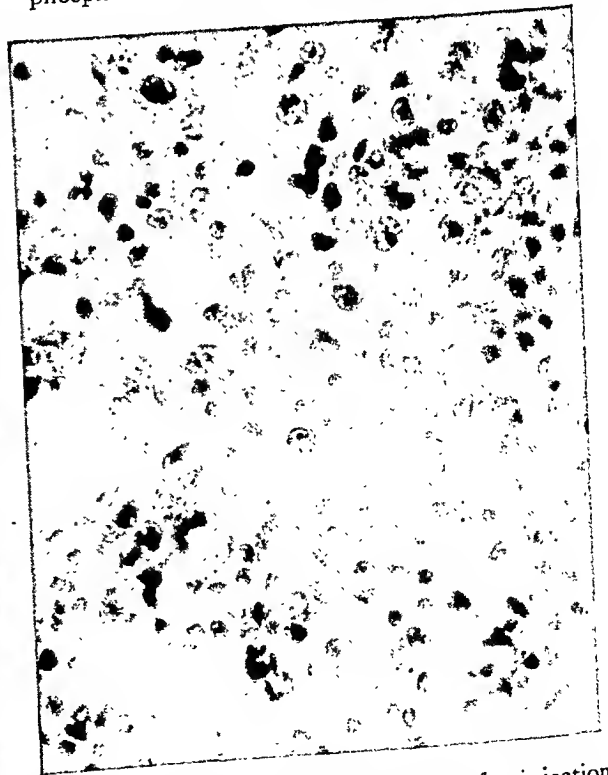


FIG. 13. Mouse lymph node 217 hours after injection with 195.3 microcuries of radiophosphorus. $\times 640$.

lymphomatous animals which received no P^{32} (see Fig. 8, 9, 10 and 11).

The chief effect of P^{32} on the lymph nodes of normal mice was a decrease in gross size and cellularity; early granulocytes were frequent and the relative proportion of large lymphocytes increased. With respect to mice receiving only lymphoma cell injection, the lymph nodes became infiltrated and increased in size eight to sixteen days later. At twenty days the infiltration of lymph nodes by lymphoma cells was very obvious. When lymphomatous mice were given P^{32} eight days after lymphoma injection, no lymphoma cell infiltration was observed until nineteen days after the introduction of lymphoma cells (see Fig. 12, 13, 14 and 15).

Studies of the spleens of normal mice seventy hours after P^{32} administration showed some lymphocytic degeneration. There was an increase of red pulp with a proportional decrease of white pulp. The megalokaryocytes appeared normal. Two

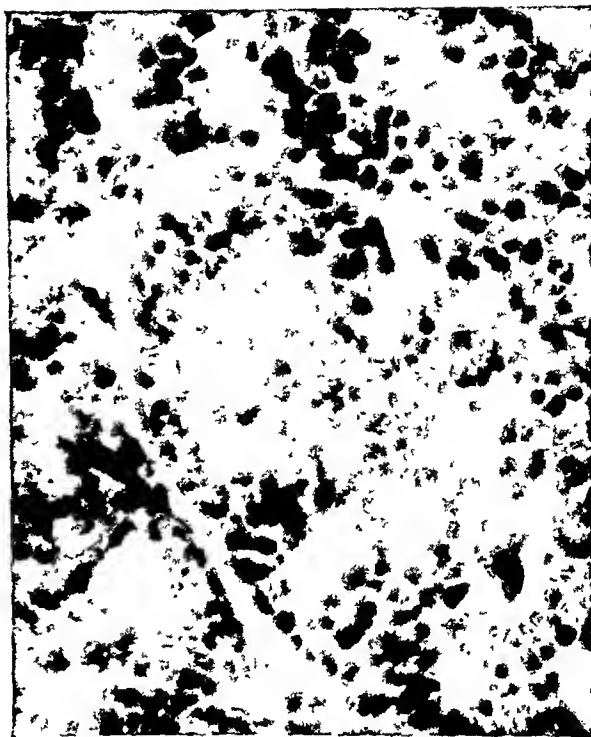


FIG. 15. Leukemic (twenty-two days) lymph node 360 hours after injection of 218 microcuries of radiophosphorus. Compare with Figure 14. $\times 640$.

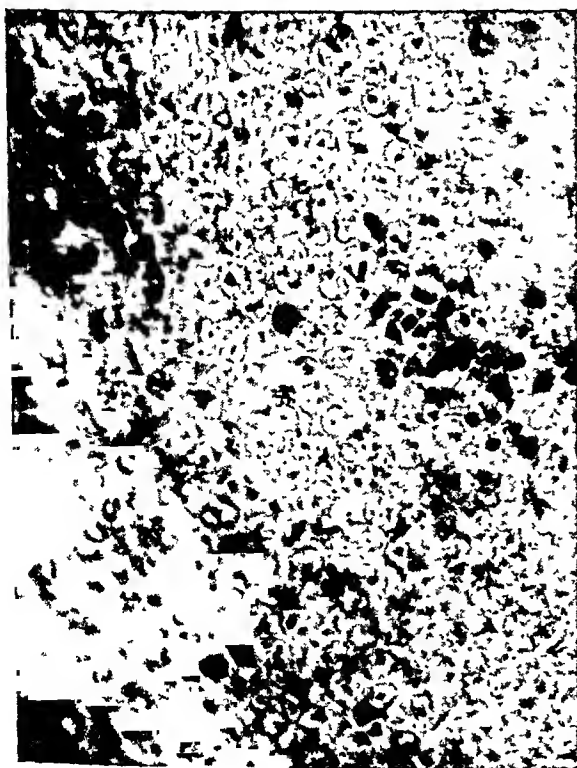


FIG. 14. Leukemic (twenty days) lymph node. Note dense leukemic cells. $\times 640$.

hundred hours after P^{32} administration the gross size of the spleen was greatly reduced. The large lymphocytes were predominant. The number of mitotic figures had decreased. Granulocytes were scarce and no megalokaryocytes could be observed.

When the mice were injected with lymphoma cells a large increase in the size of the spleen was observed twenty days later; this increase was due to invasion by lymphoma cells. Of the remaining normal lymphocytes, the large forms were predominant.

When the mice receiving lymphoma cells were given P^{32} eight days later, only slight splenic invasion by lymphoma cells was observed. At twenty days after lymphoma injection, infiltration with lymphoma cells was observed but was not as great as in the untreated leukemic animals (see Fig. 16, 17, 18 and 19).

Discussion of Histological and Hematological Results. These results show an initial depressing action of P^{32} on the lymphocyte

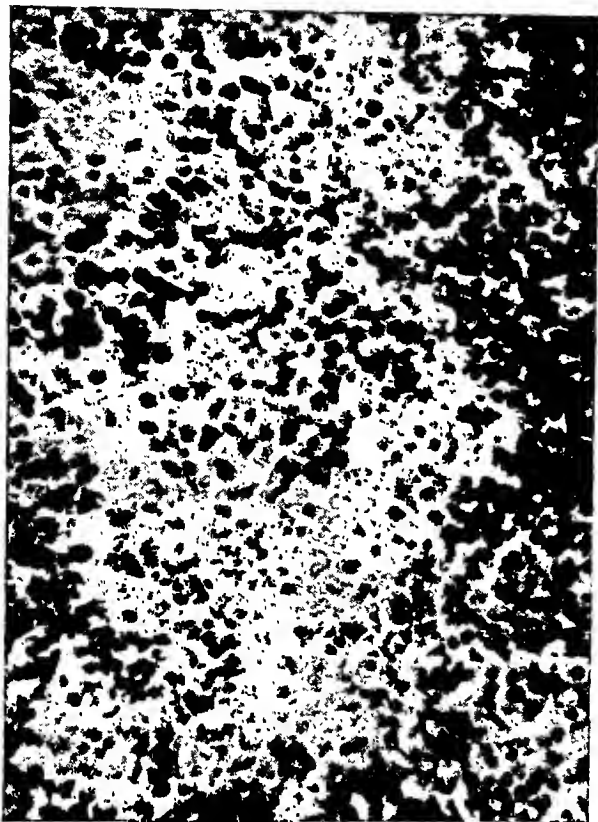


FIG. 16. Normal mouse spleen. $\times 330$.

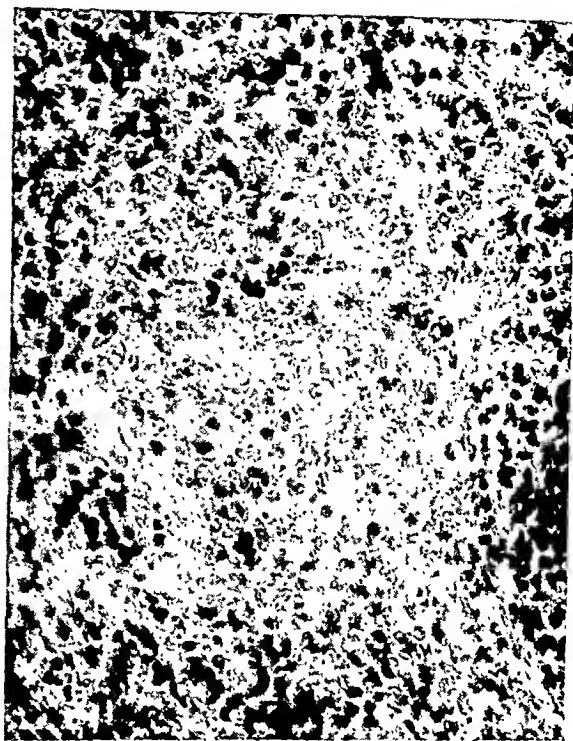


FIG. 17. Mouse spleen 214 hours after injection of 218 microcuries of radiophosphorus. Note decreased cellularity of tissue. $\times 330$.



FIG. 18. Leukemic (twenty days) spleen. $\times 330$.

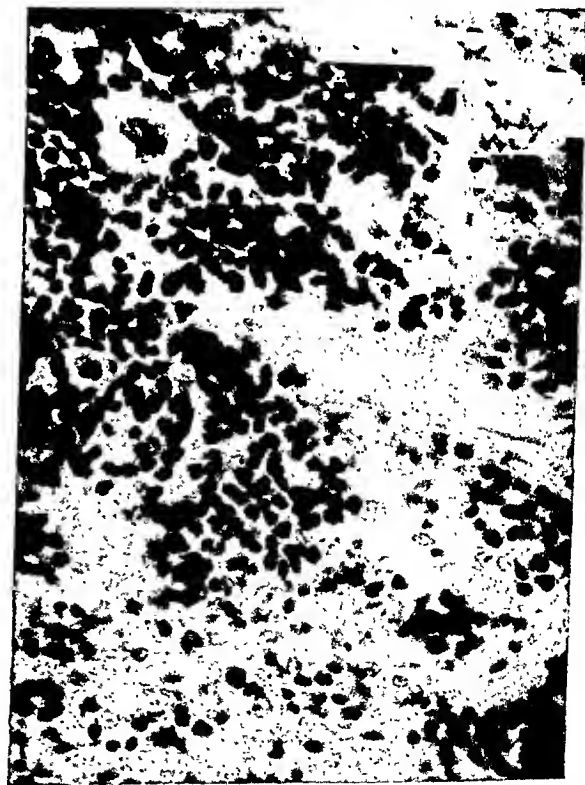


FIG. 19. Leukemic (thirteen days) spleen 140 hours after injection with 218 microcuries of radiophosphorus. $\times 330$.

series in the peripheral blood stream. After four days, when the granulocytes begin to drop off markedly, there already is an increasing deposition of P^{32} in bone. The retention of P^{32} by bone is of much longer duration than by lymphatic or any other tissue. It seems justifiable to correlate this fact with the more prolonged drop of the granulocytes. We have already noted that P^{32} seemed to have a greater initial depressing effect on the white cell count of the leukemic than on the normal animals, but there is no direct evidence that the neoplastic cells are more radiosensitive than other cells.

If the histological data on the treated and untreated lymphomatous animals are compared, we note that at corresponding stages in the lymphomatous process the treated lymphomatous animals have less infiltration of organs by leukemic cells than the non-treated groups.

We may conclude that when relatively large doses of P^{32} are given to normal and leukemic animals, the greatest drop in white blood cells occurs during the first four days after administration. The chief cell type to be affected is the lymphocyte and the lymphoma or leukemic cell. During the following five days the rate of drop is diminished, but during this period the greatest decrease in granulocytes occurs. Thereafter, there is a gradual increase in small lymphocytes and leukemic cells although the granulocytes continue to decrease in number. P^{32} delays the time of appearance of dense infiltration of tissues.

PART II

Experimental Therapy of Leukemic or Lymphomatous Mice. Studies of the exchange of P^{32} in leukemic tissues of mice revealed a higher uptake than in other soft tissues. This greater retention reached a maximum about three days after administration of P^{32} , but lymphomatous tissue retained more P^{32} as long as nineteen days after P^{32} administration when compared with normal lymph node, although

this difference tended to decrease with the passage of time.

From a therapeutic point of view this greater uptake in neoplastic tissue is of interest since these cells receive relatively more irradiation. When mice inoculated with lymphoma were given single doses of P^{32} , greater than 75 microcuries, death always resulted. At postmortem it is difficult to determine whether the mice have died from lymphoma or from radiation effects. On the other hand, we know from previous work, that the lethal dose for normal mice of these ages and weights is about 75 microcuries. In the following experiments it was decided to give the active phosphorus in several smaller doses since by this method it was hoped that activities lethal to lymphoma but sublethal to the animal could be maintained for long periods of time.

Experiment 1. The mice used were "A" strain, eight week old males. They were given intraperitoneally a suspension of lymphoma cells. All twenty of the mice developed enlarged spleens, tumors, or both, eight days later. Ten mice were used as controls and all died with evidence of generalized lymphomatosis. The other 10 mice were given P^{32} intraperitoneally* as follows: eight days after lymphoma transmission, 27.8 microcuries; eleven days, 24.2 microcuries; fifteen days, 13 microcuries. Eight of these animals died. The cause of death was doubtful in some cases (i.e., from lymphoma or radiation effects). However, 2 of these animals which had shown definite evidence of lymphoma (enlarged palpable spleens) recovered. Their spleens were no longer palpable and they were alive five months after injection of lymphoma cells and in good condition.

Experiment 2. Twenty-five "A" strain males were given intraperitoneally a lymphoma cell suspension. All of these mice developed peritoneal tumors or large spleens or both within ten days. Fifteen mice were used as controls and 10 were treated with P^{32} . In this experiment the first dosage of P^{32} (20 microcuries) was given five days after lymphoma injection. At fifteen days, 28 microcuries, and at twenty-one days, 20 microcuries of additional P^{32} were given. All

* In this and following experiments P^{32} was administered intraperitoneally as an isotonic salt of sodium phosphate.

of the control animals died of generalized leukemia. Nine of the treated animals died. One of the treated animals recovered from the lymphoma after developing mesenteric tumors and an enlarged spleen. This animal was alive six months later and appeared to be in good health with no signs of lymphoma.

Experiment 3. Twenty-five "A" strain males were given intraperitoneally lymphoma cells. Twenty were selected as takes, as evidenced by enlarged spleens or palpable intraperitoneal tumors, and 10 of these were set aside as controls. The other 5 mice subsequently developed lymphomatosis and died but were not used in this experiment. All of the control mice died with the generalized disease with an average survival time of 23.4 days. All of the animals treated with radiophosphorus also died. (Average life 26.2 days.) The radiophosphorus was given as follows: 13.75 microcuries thirteen days after injection; 13.1 microcuries fourteen days and 25.5 microcuries seventeen days; total dosage 52.35 microcuries.

Experiment 4. Twenty-one Swiss "A"* crosses were given intraperitoneally a suspension of lymphoma cells. All of the animals developed leukemia from nine to twenty days later.

A. Nine days after injection, 8 of these mice were recognized as lymphoma "takes." Four were used as controls. Four received radiophosphorus as follows: eleven days after tumor transmission, 22 microcuries; twelve days, 17.5 microcuries; and seventeen days, 20 microcuries; a total of 59.5 microcuries. One mouse, which had a markedly enlarged spleen prior to P^{32} administration, was given an additional dose of 20 microcuries at twenty days, making the total dosage 79.5 microcuries. This large spleen was observed on repeated examinations but gradually decreased in size until it appeared to be normal twenty-six days after lymphoma implantation. This animal was still alive and apparently normal five months later.

B. Later, 9 more takes were observed and 5 of these were used as controls. The remaining 4 were treated with P^{32} as follows: fourteen days after implantation, 30 microcuries; seventeen days, 7.5 microcuries; nineteen days 7.5 microcuries and twenty-five days 32 microcuries; total dosage, 77 microcuries. All of the controls died of generalized involvement and

some had large subcutaneous tumors. Three of the treated animals died showing evidence of leukemia and subcutaneous tumors. The remaining mouse, which had an easily palpable tumor mass when treatment was started, slowly recovered and five months later was in good condition and apparently free from lymphomatosis. The tumor was gradually resorbed.

The average survival time of the control mice in the entire experiment was 33.7 days, whereas survival time for the treated animals dying was 34.7 days.

Experiment 5. Twenty "A" strain mice were given lymphoma intraperitoneally. Ten controls died with a survival time of 21.8 days and the ten treated animals died with a survival time of 26.6 days. The radiophosphorus dosage was as follows: 20 microcuries thirteen days after, 2.9 microcuries seventeen days after, and 8 microcuries twenty-five days after implantation; total dosage, 30.9 microcuries.

To conclude, in the five therapeutic experiments described, regression resulted in three of them. The amount of P^{32} given varied in the different experiments, and regressions resulted when the total dosage was 65, 68, 77 and 79.5 microcuries, the time periods during which the P^{32} was administered varying from nine to sixteen days. There were regressions in 5 of 31 treated animals. Although the doses used in these experiments were sublethal, and no blood studies were carried out, it is certain that marked changes in the white and red blood cell counts occurred. In these experiments which were terminated because of the transference of the medical research activities of this laboratory to other problems in 1941, no further follow-up of the apparently cured mice was made. It is possible that their recovery (aided by the inhibitory effect of P^{32} on the neoplastic growth) from implanted lymphomatosis had conferred on them an immunity to further transplantation of this tumor into them.

Relation of These Results to the Clinical Use of P^{32} . These investigations in mice and others carried out on monkeys¹¹ demonstrate that with relatively large doses of P^{32} , the bone marrow can be wiped out.

* These were the offspring of matings of "A" strain and Swiss mice.

With sufficient doses, all elements including the platelets, white cells and red cells are affected. Thus in the treatment of leukemia with P^{32} , unless the leukemic white cells are more radiosensitive than the other elements in the marrow, it is not possible to prevent their rapid production, without at the same time inhibiting red blood cell and platelet formation.^{8,4,7} It is true that rapidly growing cells such as leukemic cells take up more P^{32} than other cells, but if these cells are adjacent to other types of cells, the latter will also receive irradiation since the beta rays from P^{32} penetrate several millimeters in tissue. In the treatment of leukemia one nearly always eventually arrives at the point where the leukemic cells become radioresistant or at least no more radiosensitive than the platelet and red cell producing centers. Thus even though there is some selective irradiation, especially by virtue of P^{32} localization in infiltrated lymph nodes, spleen and liver, one eventually faces the same problem as is faced when using spray or local roentgen irradiation since the whole marrow, and therefore both leukemic and normal elements, are being irradiated. These predominant effects of P^{32} on the various elements of the marrow constitute the limiting factor in its use in the therapy of leukemia and make its use of doubtful value in lymphosarcoma and allied diseases. Recent investigations in this laboratory indicate that it may be possible, however, to cause a relatively greater deposition of P^{32} in the tissues other than the bone marrow and thus decrease the bone marrow irradiation.

In the general problem of the radiation therapy of neoplastic disease (and leukemia may well not be a neoplasm), one should find a radio element or compound of the element which would localize to a high degree in or immediately around the neoplastic cell. There are examples of such localization in normal tissue in the case of radioactive iodine in the thyroid gland³ and chromic phosphate (radioactive phosphorus)⁵ in the liver and spleen. In these two instances it has been possible to remove in

animals the thyroids and spleens by selective irradiation without serious damage to the rest of the body. These are examples of selective irradiation in the true sense of the word. Since leukemia is such a diffuse disease, the possibilities of finding a method of true selective irradiation are not great, and for this and other reasons we must look for the control of this disease by some method other than irradiation.

SUMMARY

Hematological and histological studies on normal and lymphomatous mice which have been given radiophosphorus revealed characteristic effects on the hematopoietic tissues. Although a few animals recovered from generalized lymphomatosis after treatment with P^{32} , no evidence of any increased radiosensitivity of the neoplastic cells was observed. The limiting factors in the use of roentgen irradiation and P^{32} in the therapy of leukemia and allied diseases are discussed.

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STUDIES ON THE EFFECTS OF RADIOACTIVE SODIUM AND OF ROENTGEN RAYS ON NORMAL AND LEUKEMIC MICE*

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THE possibility of employing artificially produced radioactive substances in therapy is attractive, and various trials of some of them have been made.^{1,2} In general, it has been considered desirable to use a substance which soon after administration is selectively concentrated in certain organs. Thus radio-iodine is largely localized in the thyroid gland, radiostrontium in bone, radiophosphorus in bone, bone marrow, leukemic tissue and any rapidly growing cells. Because of this property of radiophosphorus, it has been administered in the treatment of leukemia and allied diseases, with some success.^{2,3}

This work with radioactive phosphorus is still in the experimental stage and methods of administration are tentative. The results compare favorably with those of other methods (roentgen rays and arsenic) but no great improvement has as yet been claimed. It seems that until more definite conclusions can be drawn regarding superiority of radioactive phosphorus over roentgen irradiation, it is also worth while to investigate the effects of other radioactive substances which may have some advantages.

Radioactive sodium, at the present time the most readily prepared of all these isotopes, does not concentrate in any organ or group of organs, but instead is, within a short time after its administration, distributed throughout the extracellular fluids of the body. It emits penetrating beta and gamma rays, and thus, by virtue of its distribution, can administer a rather uniform irradiation to the entire body. Its half-life, 14.8 hours, is long enough to be useful and yet short enough so that dosage can be

closely correlated with effect. Reaction to the administration of a therapeutic dose can be observed within a few days and further treatment can be regulated accordingly. Since sodium is a normal constituent of body fluids, and the radioactive isotope is administered as a small amount of isotonic saline, no physiological disturbance should occur as a result of its use, except such as would be produced by the action of the radiation. It might be expected to be valuable as a substitute or supplement for other types of irradiation in the treatment of leukemia and allied diseases.

Before using the material on human patients, it appeared desirable to study its effects on animals. Mice are particularly suitable because strains are available which exhibit a high spontaneous incidence of a condition similar to leukemia, presenting an abnormally high white blood count and enlarged lymph nodes. Accordingly, studies were undertaken with normal and leukemic mice of one of these strains, and normals of a strain which does not develop this condition. The results of the administration of radioactive sodium were compared to those of whole body roentgen irradiation. The effects to be reported at the present time are changes in blood counts and reduction in size of involved lymph nodes. Data are also presented regarding distribution of the radiosodium in various tissues and organs. A study of histologic effects is in progress and will be reported at a later date.

MATERIALS AND METHODS

The radioactive sodium, Na²⁴, was prepared by the Cyclotron Laboratory of the Physics

* With the aid of a grant from the Lilla Babbit Hyde Foundation. Presented at the Joint Meeting of the American Roentgen Ray Society and the Radiological Society of North America, Chicago, Ill., Sept. 24-29, 1944.

Department of Columbia University; it is a pleasure to acknowledge the cooperation of this group. A measured number of microcuries ($\mu\text{c.}$) of the material, in approximately isotonic sodium chloride, was injected subcutaneously in the flanks of the animal. Following such injection, the material is very rapidly distributed through all the extracellular body fluids. The gamma-ray activity of the animal was determined with a Geiger counter immediately after injection, and at intervals

entire roentgen-ray dose at one sitting. Mice of the Swiss and Ak strains were employed. The Swiss strain has been widely used for experimental studies; these were normal animals from Rockland Farms. The Ak strain, in the colony of the Crocker Laboratory (originally obtained from Dr. J. Furth, of Cornell Medical School), has a considerable incidence of spontaneous leukemia. Mrs. Mary Long, of that laboratory, supplied normal appearing mice of this strain and individuals

TABLE I
EFFECTS OF RADIOACTIVE SODIUM ON SWISS MICE

Dosage ($\mu\text{c.}$)	$\mu\text{c.}$ gram (average)	Number of Individuals	Minimum Individual White Blood Count	Duration of Leukopenia Days	Duration of Erythropenia Days	Average Survival Days
0	0	5	8,500	0	0	25 +
150	5.55	3	6,216	0	0	25 +
300	10.0	5	3,100	1	0	25 +
500	14.7	1	3,850	3	0	25 +
1,000	38.5	9	4,150	6	0	25 +
1,500	47.0	2	1,100	15	2	25 +
2,000	71.5	2	350	15	1	25 +
2,500	83.5	3	200	14	0*	20
3,000	100.0	1	150	11 +*	0*	12
4,000	125.0	1	425	7 +*	0*	8

* Does not represent total injury as animal died before the end of the experiment.

thereafter. The difference between the measured decrease in activity and the theoretical decrease due to radioactive decay represented the amount of material eliminated.

The roentgen rays were generated at 184 kv. (peak), with a filtration of 4 mm. Cu + 2 mm. Al; at a distance of 40 cm., the dosage rate was 10 roentgens per minute. During the irradiation the animals were confined in a box made of plastic material. With radioactive sodium of half-life 14.8 hours, two-thirds of the dose of radiation is delivered in the first twenty-four hours, 22 per cent in the second twenty-four, and so on. Since the object of the experiments was to make a reasonable comparison between the effects of this material and of roentgen rays, the dose of the latter was divided, 70 per cent being given the first day and the remainder twenty-four hours later. Of course this division is not strictly comparable with the continuous irradiation from the sodium, but it was felt to offer a better approximation to it than administering the

with varying types of the disease. Blood for counts was taken from the tail. Micropipettes were used and care was taken to stop the loss of blood after samples were removed.

EXPERIMENTAL RESULTS

1. *Effects on Normal Swiss Mice of Different Doses of Radioactive Sodium.* Twenty-seven animals were injected with amounts of radioactive sodium varying from 150 to 4,000 microcuries (5.55 to 125 microcuries per gram of body weight). Survival time, and white and red blood counts for this group are summarized in Table I. Controls consisted of 2 non-injected animals, 2 animals injected with isotonic non-radioactive saline, and one injected with a sample of the originally radioactive material, after its activity had decayed to a negligible amount. In no case did any of these animals exhibit any unusual change in its blood count.

The treated animals were sacrificed twenty-five days after the injection of the radiosodium, if they survived that long. Doses of 3,000 and 4,000 microcuries were

the duration of leukopenia* was increased, to a maximum of about fifteen days, and the average survival time was diminished. Erythropenia occurred only after relatively

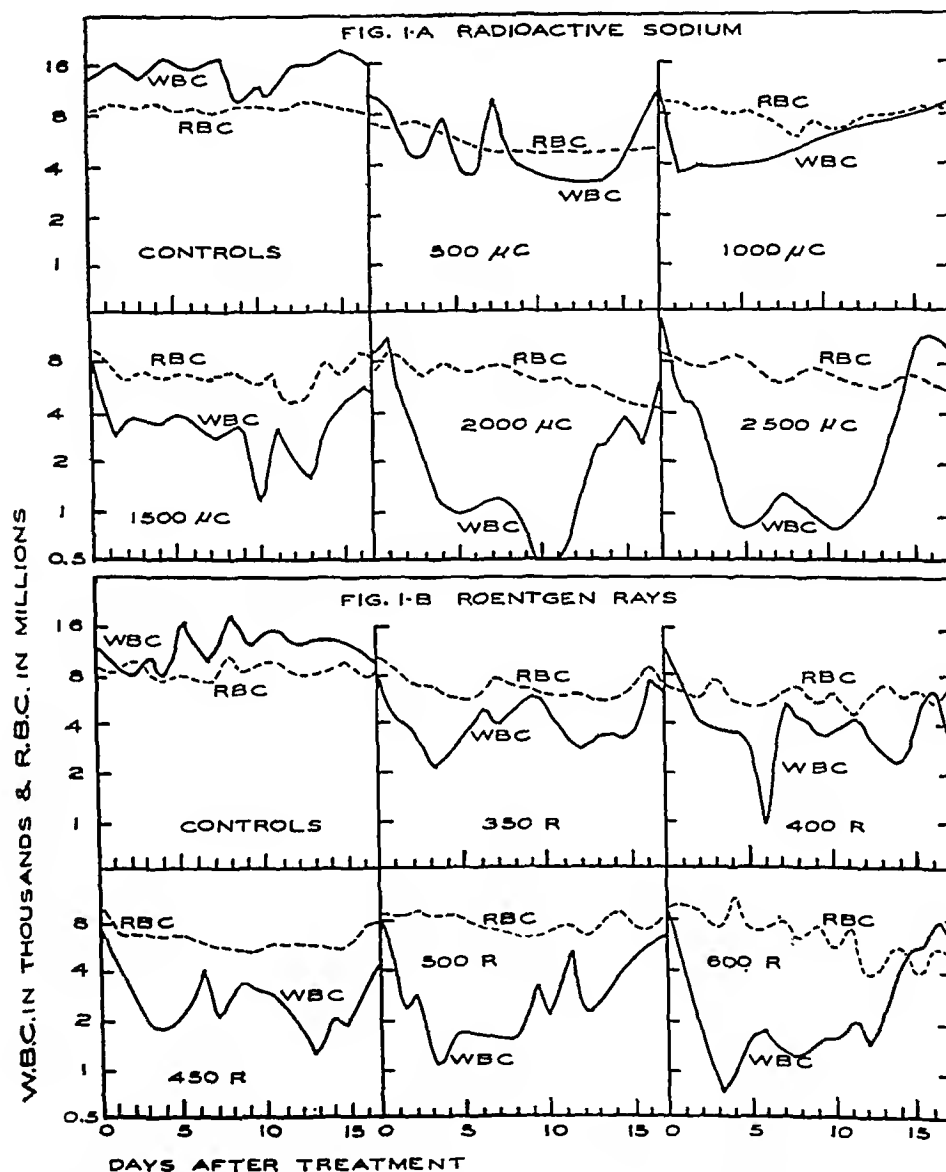


FIG. 1. A, changes in the erythrocyte and leukocyte counts of mice following treatment with radioactive sodium. B, changes in erythrocyte and leukocyte counts following roentgen irradiation. Daily determinations were alternated between two animals of each graph. For further details see text and Tables I and II.

fatal in less than two weeks, and of the 3 animals receiving 2,500 microcuries, 1 died in ten days. A temporary reduction in leukocyte count was produced by a dose as low as 300 microcuries. As indicated in the table, with increase in dosage the minimum individual white blood count was lowered;

large doses, and does not appear as soon as leukopenia.

The average daily white and red blood counts of these animals are shown in Figure

* For purposes of this study, a white blood count of 5,000 or below is called leukopenia; a red blood count of 5,000,000 or below is called erythropenia.

1A. Since the individual fluctuations are great, a logarithmic scale has been adopted to smooth out small variations and emphasize significant changes. The increase in degree and duration of leukopenia with increased dose is evident, as is also the fact that in animals of this strain considerable depression in the white blood count may be

dose administered one day and 30 per cent the next; the results are shown in Table II and Figure 1B. The curves of Figure 1B closely resemble those of Figure 1A, indicating that the effects of the two treatments are of the same kind. From Table II it is also evident that as the dosage is increased the leukopenia becomes more pro-

TABLE II
EFFECTS OF ROENTGEN IRRADIATION ON SWISS MICE

Dosage (Roentgens)	Number of Individuals	Minimum Individual White Blood Count	Duration of Leukopenia Days	Duration of Erythropenia Days	Average Survival Days
0	2	8,000	0	0	25+
350	2	2,000	8	0	25+
400	2	1,000	9	1	25+
450	2	1,250	13	2	25+
500	2	900	14	0	25+
600	2	650	15	2	25+
700	2	500	15	4	25+
800	3	250	15	4	11
900	3	300	15	4	16
1,000	1	300	Died at 5 days		5

produced with no noticeable effect on the red blood count during this period.

2. *Effects on Normal Swiss Mice of Different Doses of Roentgen Rays.* Nineteen animals were exposed to doses of from 350 to 1,000 r of roentgen rays, 70 per cent of the

nounced and prolonged, to a maximum duration of about fifteen days, erythrocytes are reduced in number, and finally survival is affected.

Not only do radiosodium and roentgen rays have similar effects on total white and red blood counts, but they also produce similar changes in the differential counts. Lymphocytes are more radiosensitive than the other leukocytes; typical effects are shown in Figure 2. The percentage of lymphocytes was multiplied by the total number of leukocytes for that day to obtain the number of cells of that type per cubic millimeter of blood. At this dosage level either sort of irradiation produced a lymphopenia of approximately two weeks' duration. A minimum was reached within three days, followed by recovery. The heavier dosage (450 r) of roentgen radiation produced a lower minimum and slower recovery than did the 350 r treatment. The effects of 1,500 μ c. appear to be more nearly like those of the 450 r experiment.

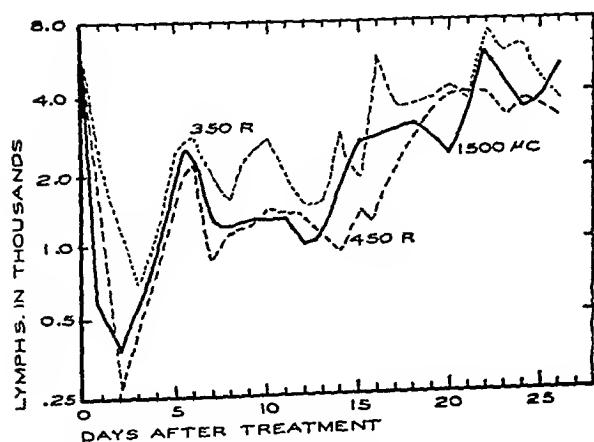


FIG. 2. Comparison of changes in leukocyte count produced by 1,500 microcuries of radiosodium (solid line) and by 350 and 450 roentgens of roentgen rays (dotted and dashed lines). See text for further details.

TABLE III

EFFECTS OF RADIOACTIVE SODIUM ON AK MICE WITHOUT LYMPHADENOPATHY

Dose μc.	Microcuries per gm.	Initial White Blood Count	Minimum White Blood Count	Duration of Leukopenia Days	Duration of Erythropenia Days	Survival Time Days
0	0	11,250	7,150	0	0	25 +
74	2.2	9,650	10,450	0	0	25 +
230	10.5	8,400	4,300	2	0	25 +
390	16	10,000	4,900	3	0	25 +
570	17	13,800	4,250	5	0	25 +
1,300	52	9,450	1,750	14	0	25 +
3,000	94	25,300	300	6*	0*	8

* Does not indicate maximum effect as animal died before end of experiment.

3. Effects of Radioactive Sodium on Mice of a Leukemic Strain.

A. Ak animals without lymphadenopathy: Before working with Ak animals with adenopathy, it was desirable to study the effects produced by radiosodium in apparently normal mice of this strain. Seven Ak animals with normal white counts and without enlarged nodes were given the same series of doses as the normal Swiss

mice. The results, given in Table III show effects similar to those in Table I. It appears that any difference in radiosensitivity between these animals and those of the same strain with lymphadenopathy may be attributed to their disease.

B. Ak animals with aleukemic adenopathy: From time to time animals with palpable nodes were found in the Ak colony. Blood counts were made on them, and those with white counts higher than 30,000

TABLE IV

EFFECTS OF RADIOACTIVE SODIUM ON AK MICE WITH ALEUKEMIC ADENOPATHY

Animal	Dose μc.	Micro- curies per gm.	Initial White Blood Count	Mini- mum White Blood Count	Duration of Leuko- penia Days	Duration of Erythro- penia Days	Sur- vival Time Days	Nodes 0 day	Nodes 1 week	Nodes 2 weeks
Ak35	0	0	10,200	4,000	1	0	14 +	Medium	Medium	Medium
Ak33	0	0	8,700	6,300	0	1	14 +	Small	Small	Small
Ak3	150	6	12,350	10,800	0	0	14 +	Medium	Small	Very small
Ak2	146	5	15,500	9,500	0	0	14 +	Medium	Small	None
Ak15	170	5	23,150	11,600	0	0	14 +	Medium	Very small	Very small
Ak5	170	5	9,650	13,400	0	0	14 +	Medium	Small	Small
Ak6	164	5	11,900	8,100	0	0	14 +	Medium	Small	None
Ak10	345	13	9,830	3,000	2	0	14 +	Very small	None	None
Ak27	514	14	23,250	3,600	3	0	14 +	Very small	None	None
Ak29	510	17	25,850	4,500	1	3	14 +	Small	None	Very small
Ak11	660	21	16,800	3,800	2	0	14 +	Very small	None	Very small
Ak34	800	28	22,500	2,950	2	0	14 +	Large	None	Very small
Ak12	1,000	29	16,950	3,000	1	0	14 +	Small	None	Small
Ak26	1,014	30	25,350	3,750	3	0	14 +	Medium	Very small	Small
Ak22	920	32	12,250	1,700	2	0	14 +	Medium	Small	None
Ak8	1,250	40	7,550	1,800	14	1	14 +	Large	Small	Small
Ak31	1,450	68	11,350	1,650	3	0	14 +	Large	Very small	None
Ak13	3,000	94	11,800	350	4(death)	4(death)	4	Large	Small	—

were considered leukemic, those with lower counts, aleukemic. Eighteen animals of the latter type have been given radiosodium; the results are shown in Table IV. The minimum white blood counts corresponded roughly to those of normal animals receiving the same doses. The duration of leukopenia was the same or slightly less than in

some of the mice received additional treatment and were no longer suitable for the comparison with singly treated normals.) Doses of the order of 20 microcuries per gram produced marked leukopenia, usually of rather short duration. The white count recovered rapidly to normal limits, but rarely exceeded the maximum normal level

TABLE V
EFFECTS OF RADIOACTIVE SODIUM ON AK MICE WITH LEUKEMIC ADENOPATHY

Animal	Dose μ c.	Micro- curies per gm.	Initial White Blood Count	Mini- mum White Blood Count	Dura- tion Aleuk- emia Days	Dura- tion Leuko- penia Days	Dura- tion Eryth- ropenia Days	Sur- vival Time Days	Nodes 0 day	Nodes 1 week	Nodes 2 weeks
Ak17	0	0	50,000	32,000	2	0	0	14+	Medium	Large	Very large
Ak23	0	0	28,500	21,700	1	0	1	14+	Large	Large	Very large
Ak39	500	14	77,000	17,250	4	0	1	14+	Very large	Medium	Very large
Ak36	500	19	141,500	2,000	8	1	10	14+	Large	Very small	Very small
Ak7	590	20	32,000	1,400	14	3	0	14+	Large	Small	Small
Ak25	604	21	38,750	4,250	14	0	0	14+	Very small	None	None
Ak24	651	24	55,000	5,250	14	1	3	14+	Small	None	None
Ak20	990	32	38,300	600	14	11	0	14+	Large	Medium	Very small
Ak30	1,444	51	46,800	1,150	14	11	10	14+	Large	Very small	Very small
Ak19	1,767	58	42,100	100	10	8	1	11	Large	None	Very small
Ak16	3,000	100	53,750	200	12	11	10	12	Large	None	None

the normals. The lymph nodes responded, at least temporarily, to doses so small as to have no apparent effect on the blood count. The effect on the nodes naturally became more pronounced as dosage increased.

C. Ak animals with leukemic adenopathy. Eleven mice had palpable nodes and white blood counts above 30,000. Some of these had low red blood counts and were weak. All animals in this group were very sensitive to the radiation, as shown by the results in Table V. (Since the initial response to a single dose of radiation was the principal point of this study, detailed data are given for only fourteen days. After that,

(30,000) during the fourteen day period. Erythropenia occurred more frequently and with lower doses than in the case of any non-leukemic group. Decrease in size of nodes was marked.

There was less uniformity in response of these animals than in the others. Figure 3 shows lymphocyte and polymorphonuclear* counts for 6 mice receiving approximately the same amounts of irradiation (see Tables IV and V for details). All had palpable nodes. Animals Ak36, 39 and 25 had unusually high lymphocyte counts. The number of polymorphonuclears and

* Includes all granulocytes.

lymphocytes of Ak27 were within control limits. Animals Ak29 and 24 had high polymorphonuclear counts. In general, they show more reduction in lymphocyte number than was produced by comparable amounts of irradiation in control animals. In

of control animals, the differential susceptibility was not as evident as that of hyperplastic lymphocytes. The susceptibility of the blood cells apparently was related to the character of the disease and the physical condition of the animal. Ak36 was the

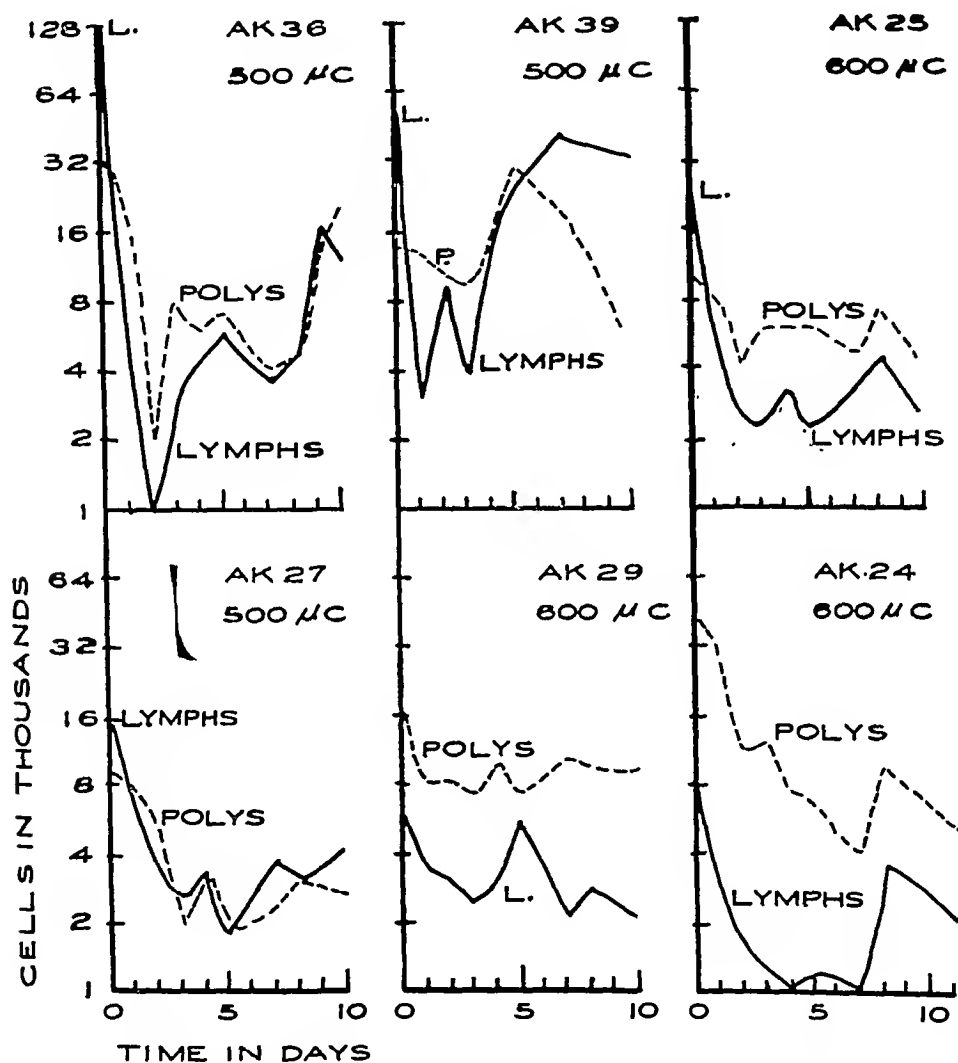


FIG. 3. Effects of radioactive sodium on blood counts of Ak animals with nodes. Solid line indicates number of lymphocytes and broken line represents number of polymorphonuclears. For further details see text and Tables III and IV.

animals having a high lymphocyte count (Ak39, Ak36) lymphopenia developed rapidly but did not persist as long as it did in animals Ak25, Ak27, with a more nearly normal initial lymphocyte count. Animals Ak29 and Ak24 had a condition similar to myeloid leukemia. Although the polymorphonuclears were affected more than those

only animal in this group whose erythrocytes were reduced in number following treatment. This animal was weak at the time of treatment and it is difficult to determine whether the anemia resulted from the irradiation or was due to continuation of the disease.

4. *Elimination.* Elimination was studied

by measuring with a Geiger counter the gamma-ray activity of the animal immediately after injection, and at various times within the next seventy-two hours. The activity at any time was expressed as a percentage of the initial activity, and the values plotted as shown in Figure 4A. The

time more than an hour or two after the injection, the activity of the animal as registered by the counter was less than the theoretical amount; this is due to excretion of some sodium by the kidneys and possibly by other routes. Although there was considerable variation among individ-

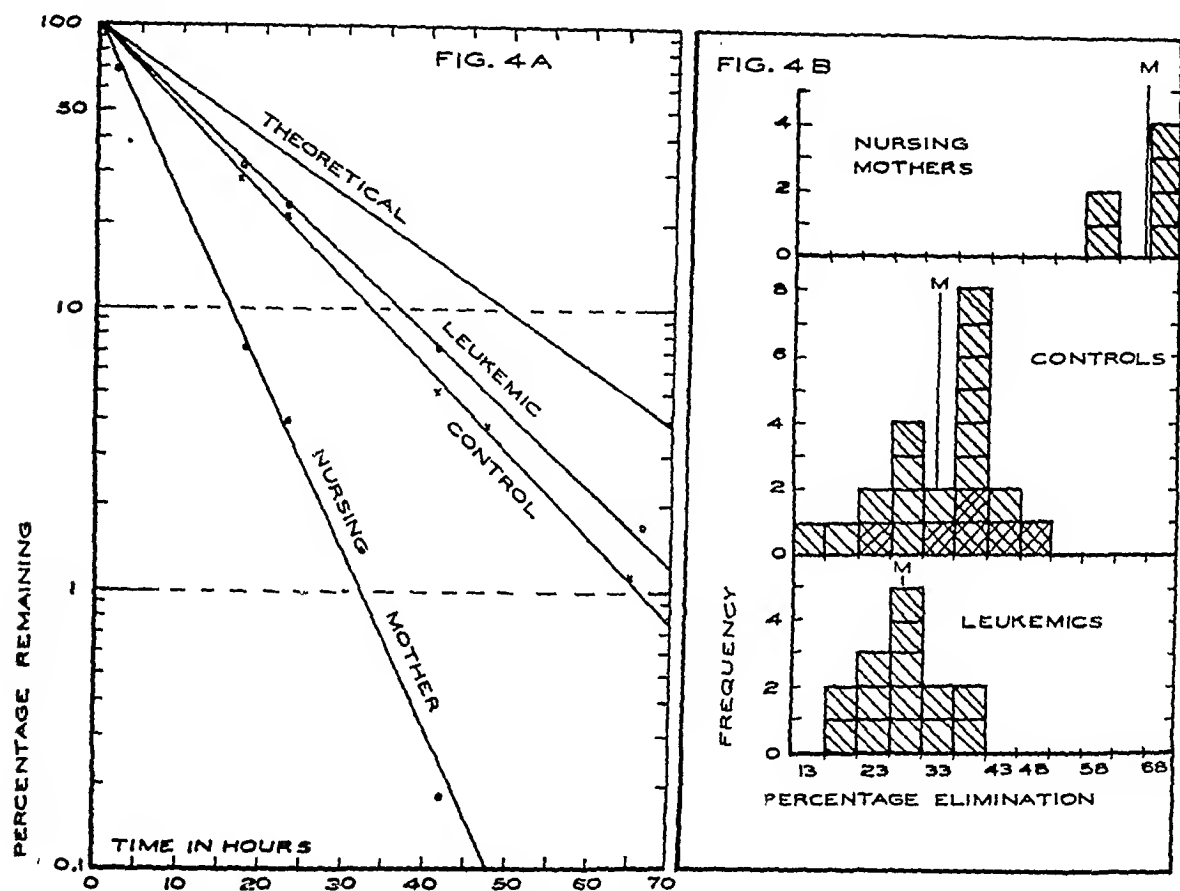


FIG. 4. A, graph showing radioactivity remaining in animals at different times following administration of radiosodium. Method of determining percentage elimination from these curves is explained in text. B, frequency graph showing individual animals grouped according to percentage elimination. Abscissa indicates percentage elimination in increments of 5 per cent. Ordinate shows number of cases in each class. In chart for controls, Swiss strain mice are indicated by singly cross-hatched blocks, non-leukemic Ak animals by doubly cross-hatched.

upper line (theoretical) is calculated from the known radioactive decay rate of Na^{24} ; from time to time the material used has been checked against this curve to be sure there was no contamination with other radioactive substances. If the animals did not eliminate any of the administered material, their activity should also follow this curve. However, it was found that at any

time more than an hour or two after the injection, the activity of the animal as registered by the counter was less than the theoretical amount; this is due to excretion of some sodium by the kidneys and possibly by other routes. Although there was considerable variation among individ-

ual animals, the points for the activity of any one at different times lie essentially on a straight line, when plotted to a logarithmic scale.

In Figure 4A are shown samples of such curves, for 1 control and 1 leukemic animal, and, for contrast, a nursing mother mouse of the Ak strain. It is impracticable to present these curves for each animal, since

those for controls and leukemics all lie together within a fairly narrow region which is definitely below the theoretical curve, indicating that appreciable elimination takes place. Due to this elimination, the effective dose of radiosodium is less than the administered amount. An approximation to the amount excreted can be obtained in the following manner: Any radioactive element has an "average life" which is 1.43 times its half-life. The total activity of 1 microcurie of the element throughout its entire lifetime, with its regularly diminishing strength, is the same as if it continued at full strength for its average life and then suddenly ceased to exist. The half-life of radiosodium is 14.8 hours; its average life is $14.8 \times 1.43 = 21.2$ hours. Hence in its total disintegration its energy can be expressed by 21.2 microcurie-hours per initial microcurie. Since the curves for the experimental animals are linear when plotted in the same manner as the theoretical one (Fig. 4A), they can be handled in the same manner as pure radioactivity curves; the situation is *as if* an element were being used which had a somewhat shorter life than sodium and was not eliminated at all. By plotting the curve for each animal to a large scale, the *effective* half-life for radioactivity in the body can be determined, and from these values the effective average lives can be calculated. The elimination is then equivalent to the difference between the theoretical and the effective average lives. For instance, the control mouse shown in Figure 4A had an effective half-life of 10 hours or an effective average life of 14.3 hours. Then instead of 21.2 microcurie-hours of irradiation per microcurie, this animal received 14.3 microcurie-hours. This means a loss by elimination of the effect of $21.2 - 14.3 = 6.9$ microcurie-hours per microcurie; $(6.9/21.2) = 33$ per cent.

Since there were relatively few animals in the experiment and considerable individual variation in the elimination percentage, average values are of little significance. Therefore a frequency graph was con-

structed (Fig. 4B) in order to compare data on this subject. The animals were grouped in steps differing from each other by 5 points (10-14, 15-19, etc.); the value for the mean of each group appears on the chart. Casual inspection leads to the conclusion that, on the average, the leukemics did not eliminate quite as much as the controls; however, the difference is found to be not statistically significant. Nursing mothers, on the other hand, do exhibit a significantly greater elimination, as might be expected, since these animals secrete sodium in the milk as well as in the urine. The radioactive sodium could be detected in the suckling babes within an hour of the time it was administered to the mother. This finding (that administered sodium is rapidly secreted in the milk) is in agreement with results obtained with humans.⁶

5. *Distribution of Radioactive Sodium in Various Organs and Tissues.* Several animals were sacrificed at various times after injection, and the gamma-ray radioactivity determined for various organs per gram of wet weight. Gamma-ray measurements were made in order to eliminate differences due to absorption of beta rays within the tissues when the samples were of different sizes. For convenience all data were related to the activity of the liver as unity. The results are shown in Table VI. At the end of two hours, as would be expected, the greatest activity was found in organs rich in blood or blood vessels. Later, as the material was more uniformly distributed through the body fluids and started to enter the cells, the differences were less marked.⁷ No effort was made to squeeze the fluid out of the specimens, and the presence of varying amounts may have influenced the results considerably. It is, however, apparent that there was no considerable concentration of the material in any particular organ or tissue.

DISCUSSION

The results thus far presented indicate that the effects produced by subcutaneous injection of radioactive sodium are of the

same sort as those resulting from whole body roentgen irradiation. The physiological changes are more marked with higher doses, and the response is essentially the same in normal mice of the two strains which were tested.

On a basis of the series of normal animals treated with radioactive sodium and with roentgen rays, it is possible to estimate the

Marinelli⁴ has published a method for determining the "equivalent roentgens" due to beta radiation delivered and completely absorbed within tissues, from radioactive substances introduced into the body and remaining there for total disintegration. While Na^{24} emits both beta and gamma rays, the latter are so penetrating that they escape from the small body of the

TABLE VI
DISTRIBUTION OF RADIOACTIVE SODIUM IN VARIOUS TISSUES
RELATIVE ACTIVITY PER GRAM WET WEIGHT

Animal	Micro-curies Injected	Hours after Injection	Blood	Kidney	Skin	Spleen	Liver	Gastro-intestinal Tract	Lungs	Lymph Nodes	Sternum	Testicles	Muscle
(WX ₃ ; 2) Swiss (Na ₁ , B ₃) Ak, no nodes (Ak 45) +nodes	200 19 30	2.5 2 2	2.0 2.5	2.1 2.1 2.3	1.0 2.8 4.7	 4.5 .9	1.0 1.0 1.0	1.1 1.9	 1.36	 3.72	 2.4	 1.7 	1.2* 0.9
(WX ₃ ; 5, 6, 7, 8) Swiss (Na ₄₂) Swiss (Na ₁ , B ₁) Ak, no nodes (Ak ₁₄) Ak +nodes	126 500 19 3,110	22 22 24 24	2.6 1.8 2.0 	1.5 1.7 0.8 1.0	 1.16 1.1 1.0	1.3 1.04 2.16 1.0	1.0 1.0 1.0 1.0	1.2 1.22 1.2	2.15 1.17 	 1.2	2.0 	1.4 0.9 0.5 1.1	
(Na ₄₃) Swiss (Ak ₉) Ak +nodes (Ak ₃₇) Ak +nodes	500 337 500	48 48 45	1.9 2.7	2.1 2.0	1.3 1.8 2.2	 1.6 0.8	1.0 1.0 1.0	1.4 1.4	1.5 1.1	 2.3 0.8	 1.87	 	0.5 0.6

* Thigh, +femur, etc.

number of microcuries of the sodium which produce the same general effect as 100 r of roentgen rays.

By inspection of the curves of Figures 1 and 2, it appears that 47 microcuries of radioactive sodium per gram of body weight produced about the same effect as 450 r of roentgen rays administered under the conditions of the experiment. This gives an equivalence of 10 microcuries per gram (neglecting elimination) and 100 r, which appears to hold within the dosage ranges studied, not only for effect on total white blood count but also on differential counts.

mouse without giving up an appreciable portion of their energy, so their contribution to the physiological dose may be considered negligible. Some of the beta rays also escape from the body. An estimate of the amount thus lost can be made as follows: These beta rays are largely absorbed by 3 mm. of water (or tissue). Hence it may be assumed that all such rays originating more than 3 mm. deep within the animal will be completely absorbed; of those originating between 1.5 and 3 mm., about three-fourths will be absorbed, and of those originating within the first 1.5 mm., about one-half. If a 30 gm. mouse be regarded as an ellipsoid

of appropriate dimensions, a calculation on this basis leads to the conclusion that only about 75 per cent of the administered beta radiation is effective.

Using Marinelli's formula, it is found that with total absorption of beta rays and no absorption of gamma rays, a dose of 1 microcurie per gram of body weight of an animal should give 32 "equivalent roentgens." The biological effect would, however, be reduced to 75 per cent of this by the escape of some beta rays from the body and further to about 65 per cent of those that would be absorbed, by physiological elimination. Thus the 32 "equivalent roentgens" would be reduced to $32 \times 0.75 \times 0.65$ or 15.6. Then 10 microcuries per gram should deliver 156 "roentgens."

This is somewhat higher than the equivalence of 10 microcuries per gram to 100 roentgens deduced from the experimental data. However, the rates of administration of radiation are quite different, and the equivalence is admittedly rough. In view of all the approximations involved in both estimates, the discrepancy is not unreasonable. It indicates that the correspondence set up is not far wrong, but that there is need for both better experimental comparison and a more accurate method of deciding the portion of the theoretical dose actually effective within the animal.

The leukemic mice were more radiosensitive to the radioactive sodium than were the normals; they were not tested with roentgen rays. Their leukocyte count was reduced more rapidly than in the normals, but also recovery began to take place earlier. The question arises as to whether this is a true difference in response, or whether these mice retain more of the material, either because of less elimination, or concentration in lymph nodes, or both. In Figure 4 it is indicated that elimination in leukemics is not significantly less than in the controls. From Table VI it is evident that there is no marked concentration in lymph nodes. It is probable that, on the average, these animals, not being in as good

general condition as the normals, are more readily affected by any injurious agent, but this is hardly sufficient to explain the difference in time of showing damage and time of recovery in the two groups. The leukemic cells apparently have a different radiosensitivity from the normal white cells, because of their rapid production and their relatively undifferentiated condition.

Some of these leukemic animals with greatly enlarged nodes appeared to have a disease comparable to acute leukemia in the human. They were usually weak at the beginning of treatment and although their condition showed temporary improvement, relapse occurred fairly soon and death ensued. Necropsy usually revealed multiple nodes and leukemic infiltration of other organs. In a few cases, such as Ak36, the animal was grossly free of leukemic disease but was anemic.

Some (more chronic) cases have been treated repeatedly with small doses of radioactive sodium at weekly or monthly intervals, and a considerable percentage of these have been kept alive and in fairly good condition for six months or more. There is, however, not yet sufficient data for a report on these cases.

The results obtained in this work do not lead directly to the formulation of a method for treating human leukemia with radioactive sodium. They do indicate that by its use a generalized radiation can be administered conveniently, in effective amounts.

It must be emphasized that the equivalence of 10 microcuries administered per gram of body weight to 100 roentgens is applicable only to mice, not to larger animals or to humans. In man, this amount would give a much higher dose of radiation, for two reasons. In the first place, whereas in the mouse practically no gamma radiation is effective, and only about three-fourths of the beta radiation, in the human practically all of the beta rays and a considerable portion of the gamma rays are absorbed. Furthermore, the mouse eliminates about a third of the material in three days, while in

this period the average human excretes less than 10 per cent.⁵ It is safe to estimate that the "equivalent roentgens" from a given dose *per gram of body weight* in the human would be at least twice as much as in a mouse.

SUMMARY

The effects of radioactive sodium and of whole body roentgen irradiation on white mice have been compared. Results in reduction of white and red blood counts and in shortening of life are similar for the two types of radiation. It has been found that 10 microcuries of radioactive sodium per gram of body weight injected subcutaneously *in the normal mouse* are equivalent in effect to 100 roentgens of heavily filtered 200 kv. roentgen rays. *This ratio would not hold for the human; the same number of microcuries would be equivalent to a considerably higher number of roentgens.*

Mice with enlarged nodes and extremely high leukocyte counts were found especially sensitive to the radiosodium. They were not tested with roentgen rays. The marked response was apparently due to radiosensitivity of the abnormal leukocytes rather than to any selective concentration of the material in lymph nodes.*

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* Since the completion of this paper, a 1944 volume of *Acta Radiologica* has become available; it has been found to contain an

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article on a similar subject. (Treatment of Leukemia with Artificial Radio-Active Sodium, by Jorgen E. Thygesen, Aage Videboek, and Irgens Villaume. *Acta Radiol.* 25¹, 305-316, 1944.) In their preliminary experiments with mice, the results were inconclusive. They report animals not able to tolerate more than 1 millicurie in a single dose, which is contrary to our findings. However their experimental procedure differed from ours in several respects,—strain of mouse, type of tumor, method of administration of radio-sodium, and method of standardization of radio-sodium dosage.



AN ANALYSIS OF THE PHYSICAL FACTORS CONTROLLING THE DIAGNOSTIC QUALITY OF ROENTGEN IMAGES*

PART III. CONTRAST AND THE INTENSITY DISTRIBUTION FUNCTION OF A ROENTGEN IMAGE

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THE clarity with which a roentgen image is reproduced is governed by four principal factors: (a) the maximum resolving power of the film or screen on which the image is recorded, (b) a relatively minor parameter called the resolution coefficient, (c) the contrast exhibited between the image and its surrounding field and (d) the unsharpness of the image boundary. In previous articles of this series,^{4,5} the relationship which these factors bear to one another has been established and a detailed discussion of maximum resolving power and the resolution coefficient presented. In this and in Part IV attention will be centered on roentgen contrast.

When the term contrast is used to describe the appearance of a roentgenographic or roentgenoscopic image, reference is made to the brightness of the image relative to the brightness of the surrounding field. When the ratio of the two brightness levels is small, contrast is low; when the ratio is large, contrast is high. Visually the relationship between contrast and the brightness ratio of an image is logarithmic. Therefore, it is customary to express contrast quantitatively as

$$C = \log I_i / I_b = \log I_i - \log I_b \quad (1)$$

where I_i and I_b are the brightness levels or light intensities emitted by the image and by its surrounding field respectively.

I. FACTORS CONTROLLING ROENTGEN CONTRAST

When a roentgen-ray beam is projected

through a structure a considerable portion of the radiation is either absorbed or scattered by the various included materials. The relatively small remainder progresses through the structure to emerge unaltered from the other side. The fraction of the radiation which falls in the latter category depends among other things on the atomic composition and densities of the materials transmitting the radiation. Thus, if the structure is composed of bone, muscle and fat tissue, the roentgen-ray intensity of the emergent beam varies from point to point in a plane perpendicular to the direction of the radiation in accordance with the characteristics of the tissues through which the beam passes; that is, the emergent beam presents a series of roentgen-ray images of the various components of the structure. Since the eye does not respond to roentgen radiation, these images may only be perceived when recorded by a roentgenographic film or roentgenoscopic screen.

The brightness levels exhibited by an illuminated film or an irradiated screen are governed by the intensities of the activating roentgen radiation. Contrast, therefore, is primarily determined by the intensity distribution function of the radiation which the film or screen receives and accordingly is a function of the properties of the structure under examination and the characteristics of the roentgen beam.

The relationship between the roentgen-ray intensity transmitted by a homogeneous structure and the structure's thickness and density is illustrated graphically in Fig-

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ure 1 and may be expressed by the equation

$$\log G = \log G_0 - \int b \rho dx \quad (2)$$

where G is the intensity of the roentgen radiation transmitted by the material, G_0 is the radiation intensity if no structure were interposed in the roentgen beam, ρ and x are the density and thickness of the material respectively and b is the negative slope of the $\log G$ vs. ρx curve.

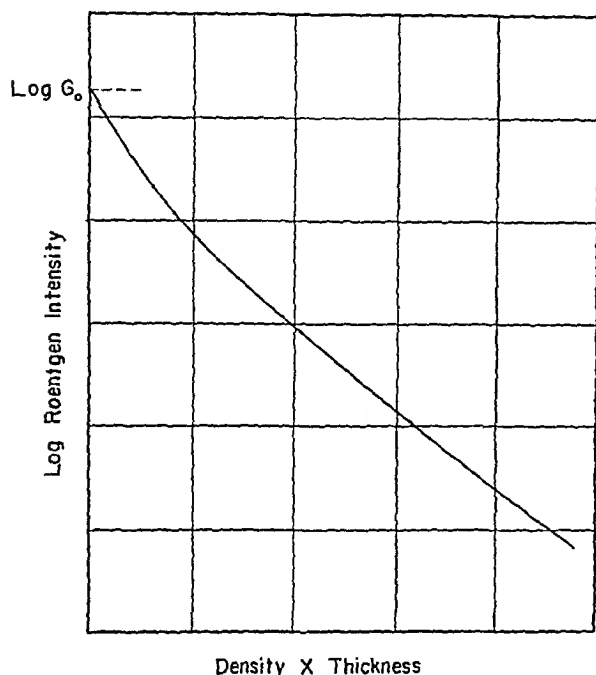


FIG. 1. Relationship between the logarithm of the roentgen-ray intensity transmitted by a structure and the product of the structure's density and thickness.

As pointed out in Part I of this series, the factor, b , is the material's mass absorption coefficient expressed in decadic logarithms. Its value is a function of the atomic numbers of the several components comprising the material and of the spectral distribution of the roentgen radiation. It thereby is a function of the voltage applied to the roentgen tube and of any filtration placed in the roentgen beam.

Equation (2) is valid only for a homogeneous structure and then only when scattered radiation is excluded from consideration. When the structure is hetero-

geneous and scattered radiation is present, the expression requires further development.

The intensity of the primary radiation transmitted by a heterogeneous structure may be related to the absorption coefficients, densities and thicknesses of the several constituents of the structure merely by expanding equation (2); that is,

$$\log G_p = \log G_0 - \int_0^{x_1} b_1 \rho_1 dx - \int_0^{x_2} b_2 \rho_2 dx \dots - \int_0^{x_n} b_n \rho_n dx \quad (3)$$

where G_p is the intensity of the primary transmitted radiation and the subscripts, 1, 2, ..., n , refer to the absorption coefficients, densities and thicknesses of the n materials included in the structure.

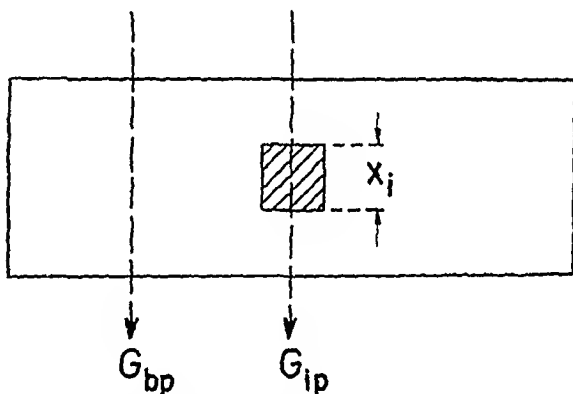


FIG. 2. Schematic diagram illustrating relationships expressed in equations (3a) and (3b).

Now, if a roentgen beam is projected through a heterogeneous structure which includes an image-producing object of thickness, x_i , and density, ρ_i , and having a mass absorption coefficient, b_i , the roentgen-ray intensity of the primary emergent beam directly below the object (see Fig. 2) is given by the equation,

$$\log G_{ip} = \log G_0 - \int_0^{x_1} b_1 \rho_1 dx - \int_0^{x_2} b_2 \rho_2 dx \dots - \int_0^{x_i} b_i \rho_i dx \dots - \int_0^{x_n} b_n \rho_n dx. \quad (3a)$$

Also if this object is surrounded by a material having a density, ρ_b , and a mass absorption coefficient, b_b , the roentgen-ray intensity of the primary emergent beam just outside the object's image is

$$\log G_{bp} = \log G_o - \int_0^{x_1} b_1 \rho_1 dx - \int_0^{x_2} b_2 \rho_2 dx \dots - \int_0^{x_1} b_b \rho_b dx \dots - \int_0^{x_n} b_n \rho_n dx. \quad (3b)$$

When equation (3b) is subtracted from equation (3a)

$$\log G_{ip} - \log G_{bp} = \int_0^{x_1} b_b \rho_b dx - \int_0^{x_1} b_1 \rho_1 dx. \quad (4)$$

Under most roentgen conditions the thickness of an image-producing object is sufficiently small so that the values of the mass absorption coefficients remain essentially constant over the integral. Under these circumstances then, equation (4) reduces to

$$\log G_{ip} - \log G_{bp} = (b_b \rho_b - b_1 \rho_1) x_1. \quad (5)$$

Equation (5) indicates the intensity distribution of the *primary* radiation within a roentgen image and its surrounding field. When scattered radiation is present the intensity distribution function is more complex and is dependent on the size and position of the image-producing object.

Although an object may have a variety of sizes and positions, only two combinations will be discussed at this time: (a) the object is small and occupies a position some distance from the roentgenographic film or roentgenoscopic screen; and (b) the object is small or large and occupies a position adjacent to the film or screen. As will be shown presently, a knowledge of these conditions will permit an estimation of the intensity distribution functions which occur under most circumstances.

(a) *Intensity Distribution Function of Image Produced by Small Object Located a Distance from Film or Screen.* When the image-producing object is small and occupies a

position more than a few centimeters from the film or screen, the intensities of the scattered radiation within the image and within the surrounding field are essentially equal (see Fig. 3) because radiation originating in adjoining portions of the structure may freely undercut the object and distribute itself uniformly over the film or screen surface. Furthermore, the scattered radiation arising in the object is dispersed widely inside and outside the image.

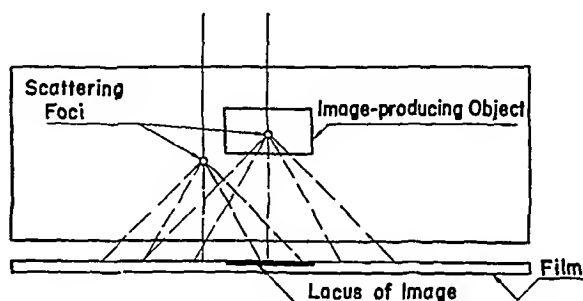


FIG. 3. Schematic diagram illustrating the dispersal of scattered radiation equally inside and outside the boundaries of a roentgen image when the image-producing object occupies a position some distance from the recording film or screen.

If the intensities of the scattered radiation within an image and its surrounding field are equal, the intensities of the total radiation at the respective sites when expressed in logarithmic form will be

$$\log G_{it} = \log (G_{ip} + G_s) \quad (6a)$$

and

$$\log G_{bt} = \log (G_{bp} + G_s) \quad (6b)$$

where G_{it} and G_{bt} are the intensities of the total radiation received within the image and its surrounding field respectively, and G_s is the intensity of the scattered radiation. Therefore, when equation (6b) is subtracted from equation (6a),

$$\log G_{it} - \log G_{bt} = -\log \left[1 + \frac{\Delta G}{G_{ip}} \left(\frac{G_{ip}}{G_{ip} + G_s} \right) \right] \quad (7)$$

where

$$\Delta G = (G_{bp} - G_{ip}).$$

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where G is the intensity of the roentgen radiation transmitted by the material, G_0 is the radiation intensity if no structure were interposed in the roentgen beam, ρ and x are the density and thickness of the material respectively and b is the negative slope of the $\log G$ vs. ρx curve.

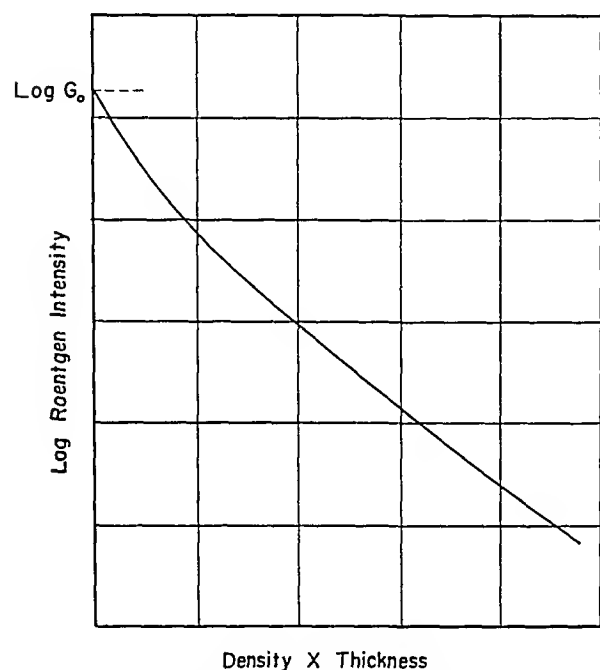


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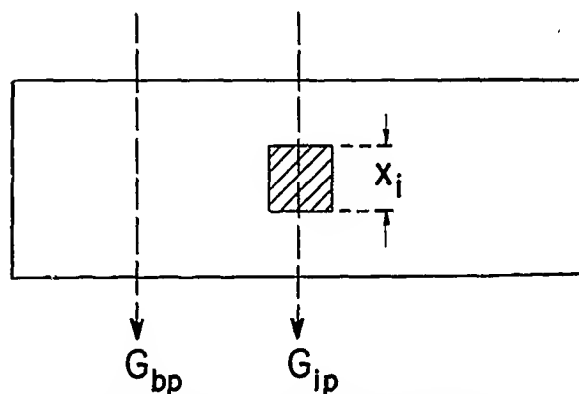


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Also if this object is surrounded by a material having a density, ρ_b , and a mass absorption coefficient, b_b , the roentgen-ray intensity of the primary emergent beam just outside the object's image is

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When equation (3b) is subtracted from equation (3a)

$$\log G_{ip} - \log G_{bp} = \int_0^{x_i} b_b \rho_b dx - \int_0^{x_i} b_i \rho_i dx. \quad (4)$$

Under most roentgen conditions the thickness of an image-producing object is sufficiently small so that the values of the mass absorption coefficients remain essentially constant over the integral. Under these circumstances then, equation (4) reduces to

$$\log G_{ip} - \log G_{bp} = (b_b \rho_b - b_i \rho_i) x_i. \quad (5)$$

Equation (5) indicates the intensity distribution of the *primary* radiation within a roentgen image and its surrounding field. When scattered radiation is present the intensity distribution function is more complex and is dependent on the size and position of the image-producing object.

Although an object may have a variety of sizes and positions, only two combinations will be discussed at this time: (a) the object is small and occupies a position some distance from the roentgenographic film or roentgenoscopic screen; and (b) the object is small or large and occupies a position adjacent to the film or screen. As will be shown presently, a knowledge of these conditions will permit an estimation of the intensity distribution functions which occur under most circumstances.

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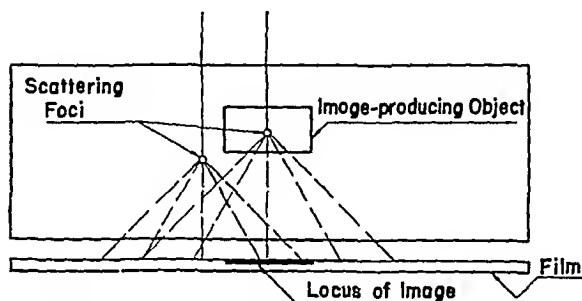


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If the intensities of the scattered radiation within an image and its surrounding field are equal, the intensities of the total radiation at the respective sites when expressed in logarithmic form will be

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and

$$\log G_{bt} = \log (G_{bp} + G_s) \quad (6b)$$

where G_{it} and G_{bt} are the intensities of the total radiation received within the image and its surrounding field respectively, and G_s is the intensity of the scattered radiation. Therefore, when equation (6b) is subtracted from equation (6a),

$$\log G_{it} - \log G_{bt} = -\log \left[1 + \frac{\Delta G}{G_{ip}} \left(\frac{G_{ip}}{G_{ip} + G_s} \right) \right] \quad (7)$$

where

$$\Delta G = (G_{bp} - G_{ip}).$$

Equation (7) may be written in the form of the power series;

$$\log G_{it} - \log G_{bt} = -\frac{1}{2.3} \left[\frac{\Delta G}{G_{ip}} \left(\frac{G_{ip}}{G_{ip} + G_s} \right) - \frac{1}{2} \left(\frac{\Delta G}{G_{ip}} \right)^2 \left(\frac{G_{ip}}{G_{ip} + G_s} \right)^2 + \dots \right]. \quad (8)$$

Under almost all roentgen conditions, the terms of this series decrease rapidly with increasing values of the exponents. Therefore, equation (8) may be written

$$\log G_{it} - \log G_{bt} = -\frac{\Delta G}{2.3 G_{ip}} \left(\frac{G_{ip}}{G_{ip} + G_s} \right). \quad (8a)$$

Also when the roentgen image is produced by a small object, ΔG is usually considerably less than G_{ip} ; therefore

$$-\frac{\Delta G}{2.3 G_{ip}} = -\log \left(1 + \frac{\Delta G}{G_{ip}} \right) \\ = \log G_{ip} - \log G_{bp} \quad (8b)$$

and

$$\log G_{it} - \log G_{bt} \\ = (\log G_{ip} - \log G_{bp}) \left(\frac{G_{ip}}{G_{ip} + G_s} \right). \quad (8c)$$

When equations (5) and (8c) are combined

$$\log G_{it} - \log G_{bt} = (b_b \rho_b - b_i \rho_i) \left(\frac{G_{ip}}{G_{ip} + G_s} \right) x_i. \quad (9)$$

Thus, the presence of scattered radiation reduces the roentgen-ray intensity distribution function of an image by an amount equal to the ratio of the primary radiation intensity to the total radiation intensity.

Equation (9) is valid both when a grid is and is not used. However, it is not in a very convenient form since entirely separate data are required for its solution under the two conditions. This difficulty may be effectively overcome by expanding the function to include the grid efficiency factor.

The efficiency of a grid is determined by its effectiveness in reducing scattered radiation and may be expressed quantitatively by the equation

$$P = \frac{\frac{G_{so}}{G_{po}} - \frac{G_{sg}}{G_{pg}}}{\frac{G_{so}}{G_{po}}} \quad (10)$$

where P is the grid efficiency factor, a parameter which henceforth will be referred to as the *Potter coefficient*,

G_{so} and G_{po} are the intensities of the scattered and primary radiation respectively when a grid is not used and

G_{sg} and G_{pg} are the intensities of the scattered and primary radiation respectively transmitted by the grid.

When equation (10) is rearranged and the factor $(1-P)$ added to each side

$$G_{sg}/G_{pg} + 1 - P = (1-P)G_{so}/G_{po} + 1 - P. \quad (10a)$$

Also when equation (10a) is rearranged and inverted

$$\frac{G_{pg}}{G_{pg} + G_{sg}} = \frac{G_{po}/(G_{po} + G_{so})}{1 + P[G_{po}/(G_{po} + G_{so}) - 1]}. \quad (10b)$$

But the left hand term of equation (10b) represents the intensity ratio of primary to total radiation occurring when a grid is employed. Therefore, when equation (10b) is substituted in equation (9), the intensity distribution function becomes

$$\log G_{it} - \log G_{bt} = \frac{(b_b \rho_b - b_i \rho_i) m x_i}{1 + P(m-1)} \quad (11)$$

where

$$m = G_{po}/(G_{po} + G_{so}).$$

It will be observed that equation (11) applies equally well to conditions where a grid is not employed if a value of zero is given the Potter coefficient, P , and therefore may be solved with but one set of scattering data regardless of the presence or absence of a grid.

(b) *Intensity Distribution Function of Image Produced by Small or Large Object Located in Apposition to the Film or Screen.* When the image-producing object is in close apposition to the film or screen, there is no opportunity for it to be undercut by scattered radiation arising in other portions

of the structure; neither is scattered radiation originating within the object permitted to disperse widely beyond the image boundaries. Accordingly the derivation of the intensity distribution function under this condition follows identically that from which equation (5) was developed with the exception that values of the mass absorption coefficients must be determined from absorption curves made under conditions where scattered radiation is present. The function is simply

$$\log G_{it} - \log G_{bt} = (b'_b \rho_b - b'_i \rho_i) x, \quad (12)$$

where the superscripts indicate the special conditions under which the mass absorption coefficients are measured.

As in the case of equation (9), equation (12) is valid both when a grid is and is not used, but is rather inconvenient because entirely separate data are required for its solution under the two conditions. Equation (12), however, is not amenable to simplification by introducing the Potter coefficient if rigorous mathematical analysis is followed. Fortunately, values of b and b' do not differ widely from one another and a close approximation of the value of a material's mass absorption coefficient, when a grid is present, may be obtained from the equation

$$b_g' = (b - b_o')P + b_o' \quad (12a)$$

where b_g' and b_o' are the mass absorption coefficients under conditions when a grid is and is not used respectively.

When equation (12a) is substituted in equation (12), the intensity distribution function becomes

$$\log G_{it} - \log G_{bt} = \{ [b_{bo}' + (b_b - b_{bo}')P] \rho_b - [b_{io}' + (b_i - b_{io}')P] \rho_i \} x. \quad (13)$$

Equation (13) is also valid for conditions when a grid is not used when a value of zero is given the Potter coefficient, P .

Equations (11) and (13) indicate the intensity distribution functions of the radiation within a roentgen image and its surrounding field for two widely different conditions. Since the objects which produce most roentgen images (e.g. a minimal tu-

berculous process) are relatively small compared to the size of the structure in which they are located and lie some distance from the roentgenographic film or screen, the intensity distribution function usually approximates that given by equation (11). There are, however, a few instances where equation (13) is applicable.

When roentgen radiation impinges on a roentgenoscopic screen the intensity or brightness of the fluorescence is directly proportional to the intensity of the activating radiation; that is,

$$I = kG \quad (14)$$

where I is the light emission of the screen, G is the intensity of the roentgen radiation and

k is a constant.

Therefore, if G_{it} and G_{bt} are the roentgen-ray intensities within an image and its surrounding field respectively,

$$\log I_i - \log I_b = \log G_{it} - \log G_{bt}. \quad (15)$$

But according to equation (1) the left-hand portion of equation (15) is the contrast exhibited by the image; furthermore, the right-hand portion is the intensity distribution function of the roentgen radiation as given by equations (11) and (13). Therefore, the contrast of a roentgenoscopic image is simply equal to the intensity distribution function within the roentgen-ray image and its surrounding field.

If the roentgen radiation is permitted to fall on a roentgenographic film or film-screen combination instead of a roentgenoscopic screen the density of the processed film will be a function of the quantity of radiation (usually referred to as the exposure) received by the film. This relationship, shown graphically in Figure 6, Part 1, may be expressed by the equation

$$D = \int g \, d \log E + K \quad (16)$$

where g is the slope of the density vs. log exposure curve,

E is the quantity of radiation received by the film and

K is a constant.

The value of the factor, g , is governed by inherent characteristics of the film and the conditions under which the film is developed. Over the small ranges of density which are usually encountered between a roentgenographic image and its surrounding field, it remains essentially constant and for these conditions equation (16) may be written

$$D = g(\log E - i) \quad (16a)$$

where i is a constant.

Now the quantity of radiation received by a film is equal to the product of the effective radiation intensity, G , and the exposure time, t ; that is,

$$E = Gt. \quad (17)$$

Therefore, equation (16a) may be written

$$D = g(\log G + \log t - i). \quad (18)$$

Furthermore, if G_{it} and G_{bt} are the intensities within a roentgen-ray image and its surrounding field respectively, the relationship between the resulting roentgenographic densities will be

$$D_i - D_b = g(\log G_{it} - \log G_{bt}) \quad (19)$$

since all portions of the film receive the same exposure time. But by definition the density of a film is a direct function of the logarithm of the light intensity transmitted by the film. Accordingly, the left side of equation (19) represents the contrast exhibited by the image; that is,

$$C_f = g(\log G_{it} - \log G_{bt}). \quad (20)$$

It is evident from equation (20) that the contrast of a roentgenographic image is simply equal to the product of g , a factor which may be conveniently called the film contrast factor, and the intensity distribution function of the roentgen radiation as given by equations (11) and (13). Indeed equation (20) is valid for both roentgenographic and roentgenoscopic images if a value of unity is given the factor, g , in the latter instance.

An examination of equations (11) and (13) reveals that the contrast of a roentgen

image is governed by a complex series of factors, including the thickness and density of the image-producing object. Also, since the mass absorption coefficient of a material is a function of the spectral distribution (quality) of the exposing radiation and of the atomic composition of the material, it is affected by the voltage applied to the roentgen tube, by filtration placed in the roentgen beam and by the absorption characteristics of the image-producing object. Finally, since the intensity ratio of primary to total radiation within an image is also a function of the size of the portal irradiated, and the efficiency of a grid if used, these factors also exert control over contrast.

II. MEASUREMENT OF FACTORS CONTROLLING ROENTGEN CONTRAST

The quantitative manner in which these factors control the contrast of a roentgen image may be evaluated from a study of data which are obtained when pertinent values are substituted in the terms of equations (11) and (13). Such values, however, are not generally available because until recently the measurement of the mass absorption coefficients of bone, muscle, fat and other tissues and of the intensity ratios of primary to total radiation occurring under various roentgen conditions has been an extremely tedious task.

Since the roentgen-ray absorption of a material is a function of the quality of the exposing radiation and since the quality of radiation encountered under roentgenographic and roentgenoscopic conditions extends through a wide range, it is essential that the instruments with which the absorption data of a material are obtained have essentially identical roentgen-ray spectral responses to those of roentgenoscopic screens and roentgenographic films exposed either with or without intensifying screens. Otherwise the results will not reflect the behavior of these screens and films when recording a roentgen image. In the past, two methods have been used to measure the roentgen-ray absorption of a material: one is the ionometric method, widely

used in roentgen therapy, in which the measurements are recorded with an ionization chamber-electrometer system; the second is the film sensitometric method in which roentgenographic film is employed as the radiation recording medium. The former is a rather simple procedure but unfortunately the spectral responses of available ionization chambers do not correspond to those of films and screens and therefore does not yield reliable information. The latter method is completely satisfactory from the standpoint of the spectral response of the recording agent if certain precautions are taken, but it presents serious difficulties when a considerable quantity of data is to be gathered because of the complexity of the procedure. For each set of conditions for which data are desired, several roentgenographic exposures must be made. The films subsequently require processing under closely identical conditions, their densities read and the results analyzed and converted to intensitometric values. It is evident that the film sensitometric method is an impractical procedure when data are to be collected through the wide range of conditions normally encountered in roentgen practice and it is not surprising that values of the absorption coefficients of various anatomical tissues and of the intensity ratios of primary to total radiation which occur under the many roentgen conditions to be expected have not been determined.

The recent development of a photoelectric roentgen-ray intensitometer³ whose spectral response may be made to coincide with that of any roentgenographic or roentgenoscopic material and with which measurements may be made quickly and easily has greatly simplified the collection of such data, however. With this instrument it has been possible to obtain much quantitative information regarding the factors which control roentgen contrast.

The measurement of the mass absorption coefficients of bone, muscle and fat cannot be conveniently conducted with living tissues and it is therefore necessary to employ substitute phantom materials whose ab-

sorption characteristics are closely similar. This problem, however, presents no serious difficulty. The mass absorption coefficient of a material is governed by the material's atomic composition and is independent of its molecular structure. Furthermore, the atomic compositions of tissues other than bone and pathological calcifications are rather similar and these structures therefore exhibit reasonably identical absorption characteristics. Accordingly, only two phantom materials, one to represent calcified and one to represent non-calcified tissues are required, and these materials, if desired, need not have chemical properties even remotely similar to the tissues for which they substitute.

Masonite presdwood, a cellulose building material having a density of 1.07, exhibits absorption characteristics similar to fat, muscle and connective tissue and, as will be pointed out presently, constitutes an excellent phantom material to represent these structures. A suitable phantom material to represent the inorganic constituents of bone and of other calcifications is also readily obtainable. It has been shown² that these constituents occur as carbonate apatite having the formula $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6 \cdot \text{H}_2\text{O}$. Accordingly a powdered mixture of calcium phosphate and calcium carbonate in proportions by weight of 9.3 to 1.0 will possess comparable absorption characteristics.

Absorption measurements have been made with both of these phantoms through a wide range of conditions in the laboratories of The University of Chicago and the United States Public Health Service. In the case of Masonite presdwood, a phantom 30 cm. square and ranging in thickness from 0 to 30 cm. was employed. Data were obtained with the roentgen machine, a four-valve, full-wave, single-phase unit operating at 30, 50, 70 and 85 kv. (peak), and with an inherent tube filtration of 0.5 mm. Al. The measurements were repeated with an added filter of 5.0 mm. Al. The sizes of the portal irradiated were 300 sq. cm. and 900 sq. cm. measured at the level

of the photoelectric intensitometer; in addition, a set of data was obtained under conditions when essentially no scattered radiation was permitted to reach the intensitometer. Under each circumstance for which an absorption measurement was

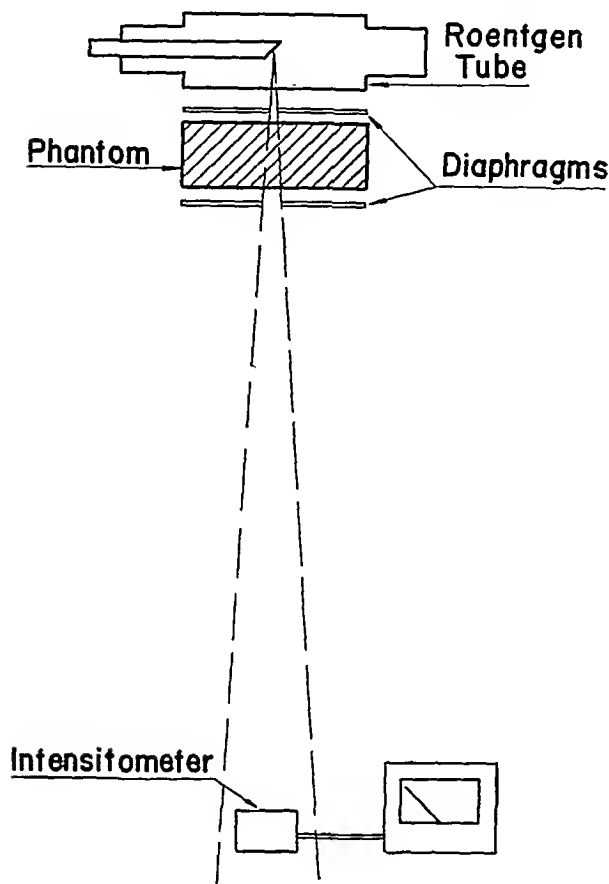


FIG. 4. Schematic diagram illustrating the arrangement by which absorption measurements were made in the absence of scattered radiation. The lead diaphragms limit the size of the roentgen beam to levels at which the quantity of scattered radiation is a minimum, and the large phantom-intensitometer distance attenuates the small quantity of scattered radiation that is produced to insignificantly low levels (less than 1 per cent of the intensity of the primary radiation).

made, readings were taken both when the intensitometer was adjusted to have a spectral response similar to that of roentgenographic films exposed with intensifying screens and when adjusted to have a response identical to that of films exposed directly to roentgen radiation. Films exposed with intensifying screens have absorption

characteristics similar to those of photo-fluorographic films exposed with a Patterson type B screen and to those of Patterson type B roentgenoscopic screens.³ The data obtained with the intensitometer having a film-screen spectral response are therefore also applicable to these conditions. Furthermore, films exposed with roentgen rays directly have a spectral response identical to that of photofluorographic films exposed with the Patterson type D screen (photo-roentgen); the non-screen data are therefore applicable to this condition.

The absorption measurements in which scattered radiation was prevented from falling on the intensitometer were made under conditions illustrated in Figure 4. It will be observed that the phantom was located at a position close to the roentgen tube whereas the radiation detector of the photoelectric intensitometer was placed 2 meters below. In addition, the roentgen beam was carefully diaphragmed above and below the phantom to reduce the production and dispersal of scattered radiation. Intensitometric measurements with the phantom located at various positions between the radiation detector and the roentgen tube indicated that the intensity of the scattered radiation when the phantom was located in the position shown in Figure 4 was less than 1 per cent of that of the primary radiation. This method of effectively eliminating scattered radiation was first suggested by Seemann.⁶

The absorption data for various thicknesses of presdwood, irradiated at roentgen tube potentials of 30, 50, 70 and 85 kv. (peak) through portals of 0.0, 300 and 900 sq. cm., with a roentgen beam filtration of 0.5 mm. Al (inherent tube filtration) and with the photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed with intensifying screens are illustrated graphically in Figure 5. Similar data, obtained with a roentgen beam filtration of 5.5 mm. Al are presented in Figure 6. In Figures 7 and 8 the data apply to conditions where films are exposed to roentgen rays directly; in the former

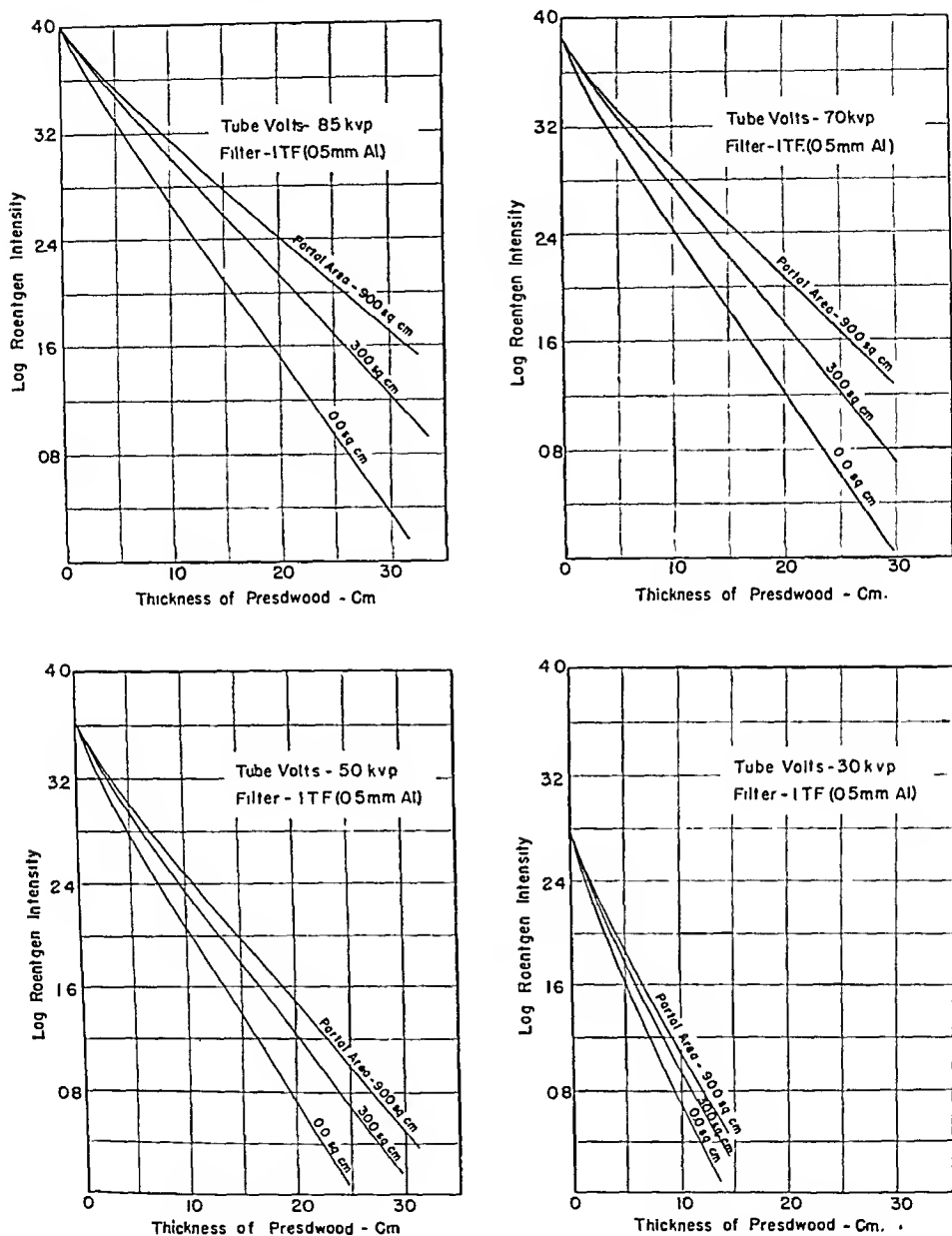


FIG. 5. Absorption curves for Masonite presdwood (density = 1.07) irradiated with a four-valve, full-wave rectified roentgen generator operating at potentials of 30, 50, 70, and 85 kv. (peak), through portals of 0.0, 300 and 900 sq. cm., with a roentgen-ray beam filtration of 0.5 mm. Al (inherent tube filtration) and with the photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed with intensifying screens.

case, readings were made with an inherent tube filtration of 0.5 mm. Al, and in the latter, with a total filtration of 5.5 mm. Al. The portal size of 0.0 sq. cm. refers to the condition where scattered radiation was prevented from reaching the intensitometer. Since in practice an absence of scattered radiation can occur only when the portal size is zero, this method of designation has been adopted.

The values of the mass absorption coefficient of Masonite presdwood under conditions when scattered radiation is prevented from reaching the film or screen (i.e. values which are applicable to equation (11)) may be determined by simply measuring the slopes of the 0.0 sq. cm. curves of Figures 5 to 8. These values are tabulated in Tables I to IV. In Table I, the data are presented for various thicknesses of presdwood when

TABLES I-IV

MASS ABSORPTION COEFFICIENTS OF MASONITE PRESWOOD EXPRESSED IN TERMS OF DECADIC LOGARITHMS
THESE VALUES ARE CLOSELY EQUIVALENT TO THOSE OF ALL ANATOMIC MATERIALS WITH
THE EXCEPTION OF CALCIFIED TISSUES

TABLE I

Data applicable to conditions where:

Exposures made with intensifying screens.
Filtration in roentgen beam = Inherent tube filtration (0.5 mm. Al)

Thickness of Presdwood (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	0.210	0.231	0.262	0.300
2.5	0.129	0.143	0.163	0.205
5.0	0.117	0.125	0.136	0.173
7.5	0.110	0.114	0.125	0.165
10.0	0.109	0.113	0.124	0.164
12.5	0.108	0.112	0.123	0.164
15.0	0.107	0.111	0.122	
17.5	0.107	0.110	0.121	
20.0	0.106	0.109	0.120	
22.5	0.106	0.109	0.119	
25.0	0.105	0.108	0.118	
27.5	0.105	0.108	0.117	
30.0	0.104	0.107	0.117	

TABLE II

Data applicable to conditions where:

Exposures made with intensifying screens.
Filtration in roentgen beam = Inherent tube filtration (0.5 mm. Al) plus 5.0 mm. Al

Thickness of Presdwood (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.107	0.110	0.125
2.5	0.105	0.109	0.120
5.0	0.104	0.108	0.118
7.5	0.104	0.108	0.117
10.0	0.103	0.107	0.117
12.5	0.103	0.107	0.117
15.0	0.103	0.107	0.117
17.5	0.103	0.107	0.117
20.0	0.103	0.107	0.117
22.5	0.103	0.107	0.117
25.0	0.103	0.107	0.117
27.5	0.103	0.107	0.117
30.0	0.103	0.107	0.117

TABLE III

Data applicable to conditions where:

Exposures made without intensifying screens
(cardboard holders).
Filtration in roentgen beam = Inherent tube filtration (0.5 mm. Al)

Thickness of Presdwood (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	0.235	0.255	0.283	0.330
2.5	0.142	0.155	0.175	0.220
5.0	0.125	0.133	0.145	0.180
7.5	0.117	0.121	0.130	0.168
10.0	0.113	0.117	0.127	
12.5	0.110	0.115	0.125	
15.0	0.108	0.112	0.123	
17.5	0.107	0.110	0.122	
20.0	0.106	0.110	0.121	

TABLE IV

Data applicable to conditions where:

Exposures made without intensifying screens
(cardboard holders).
Filtration in roentgen beam = Inherent tube filtration (0.5 mm. Al) plus 5.0 mm. Al

Thickness of Presdwood (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.110	0.120	0.132
2.5	0.106	0.113	0.125
5.0	0.104	0.111	0.120
7.5	0.103	0.108	0.118
10.0	0.103	0.107	0.117
12.5	0.103	0.107	0.117
15.0	0.103	0.107	0.117
17.5	0.103	0.107	0.117
20.0	0.103	0.107	0.117

irradiated at the four kilovoltages studied, under conditions where the radiation is received by films exposed with intensifying screens. Similar data for conditions where the roentgen beam filtration is 5.5 mm. Al are listed in Table II. Tables III and IV are

for conditions where the radiation is received by films exposed without intensifying screens; the former applies to a roentgen beam filtration of 0.5 mm. Al and the latter to a filtration of 5.5 mm. Al.

The values of the mass absorption coeffi-

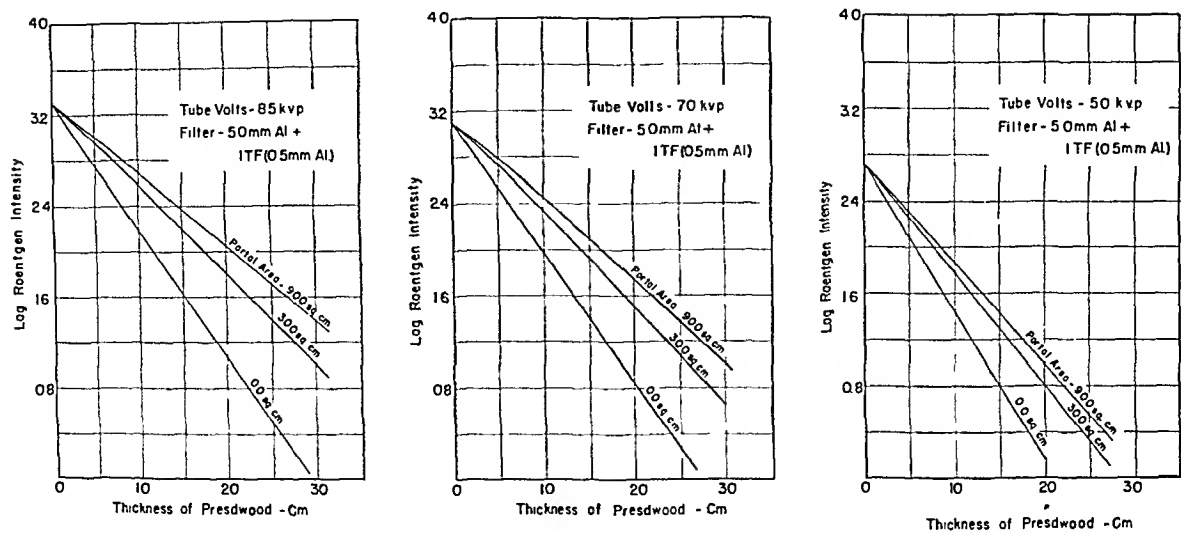


FIG. 6. Absorption curves for Masonite presdwood (density = 1.07) irradiated with a four-valve, full-wave rectified roentgen generator operating at potentials of 50, 70 and 85 kv. (peak), through portals of 0.0, 300 and 900 sq. cm., with a roentgen-ray beam filtration of 5.5 mm. Al and with the photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed with intensifying screens.

cients for presdwood listed in Tables I to IV are not, of course, exactly representative of those of bone, muscle, fat and other tissue. They are, however, closely similar as will be evident from Figure 9 where absorption curves for fresh skeletal muscle (beef), presdwood, and lard (animal fat), are plotted for roentgen tube potentials of 30, 50, 70 and 85 kv. (peak). These measurements were obtained under conditions where the intensity of the scattered radiation reaching the intensitometer was effectively zero and where the intensitometer's spectral response was similar to that of films exposed with intensifying screens. The comparative values of the absorption coefficients of the three materials at the four kilovoltages are listed in Table V, a value of 100 per cent being assigned to Masonite presdwood in each case.

The data provided in Figures 5 to 8 may also be used to calculate the intensity ratios of primary to total radiation which occur under roentgenographic and roentgenoscopic conditions for portal areas of 300 and 900 sq. cm. The values for conditions where films are exposed with intensifying screens are listed in Tables VI to IX and for conditions where films are exposed to roentgen rays directly in Tables X to XIII. In each

case the figures apply respectively to (1) a portal area of 300 sq. cm. and a roentgen beam filtration of 0.5 mm. Al (inherent), (2) a portal area of 300 sq. cm. and a total filtration of 5.5 mm. Al, (3) a portal area of 900 sq. cm., and 0.5 mm. Al filtration (in-

TABLE V COMPARATIVE VALUES OF THE MASS ABSORPTION COEFFICIENTS OF ANIMAL FAT, PRES- WOOD AND SKELETAL MUSCLE				
Material	Kilovoltage (peak)			
	30	50	70	85
Animal fat	0.92	0.94	0.96	0.97
Masonite presdwood	1.00	1.00	1.00	1.00
Skeletal muscle	1.04	1.03	1.02	1.02

herent) and (4) a portal area of 900 sq. cm. and 5.5 mm. Al filtration (total). Absorption curves for $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6$, (density = 1.00) irradiated at roentgen tube potentials of 30, 50, 70 and 85 kv. (peak), with a roentgen beam filtration of 0.5 mm. Al (inherent tube filtration) with the photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed with intensifying

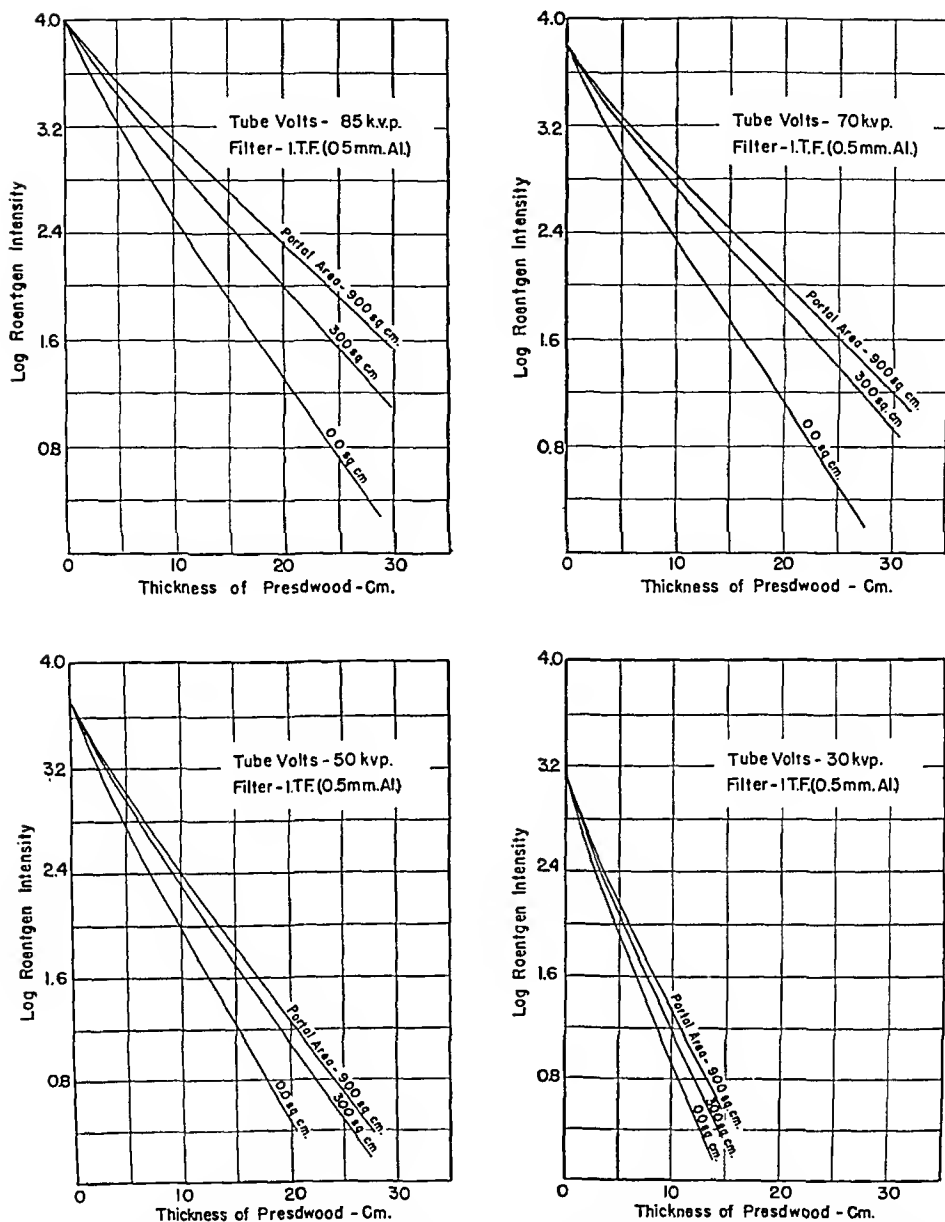


FIG. 7. Absorption curves for Masonite presdwood (density = 1.07) irradiated with a four-valve, full-wave rectified generator operating at potentials of 30, 50, 70, and 85 kv. (peak), through portals of 0.0, 300 and 900 sq. cm., with a roentgen-ray beam filtration of 0.5 mm. Al (inherent tube filtration) and with the photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed to roentgen rays directly.

screens and with scattered radiation reaching the intensitometer effectively reduced to zero are illustrated in Figure 10. Curves A to F refer respectively to conditions where additional filters of Masonite presdwood (density 1.07) 0.0 cm., 2.5 cm., 5.0 cm., 10 cm., 20 cm., and 30 cm. in thickness are present. Similar data obtained with a roentgen beam filtration of 5.5 mm. Al are shown in Figure 11. In Figures 12 and 13 the data apply to conditions where films are

exposed to roentgen rays directly; in the former case, readings were made with an inherent tube filtration of 0.5 mm. Al, and in the latter with a total filtration (exclusive of presdwood) of 5.5 mm. Al.

In Tables xiv to xxxiii are listed the values of the mass absorption coefficient of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6$ which occur under the foregoing conditions. They were determined simply by measuring the slopes of the curves in Figures 10 to 13.

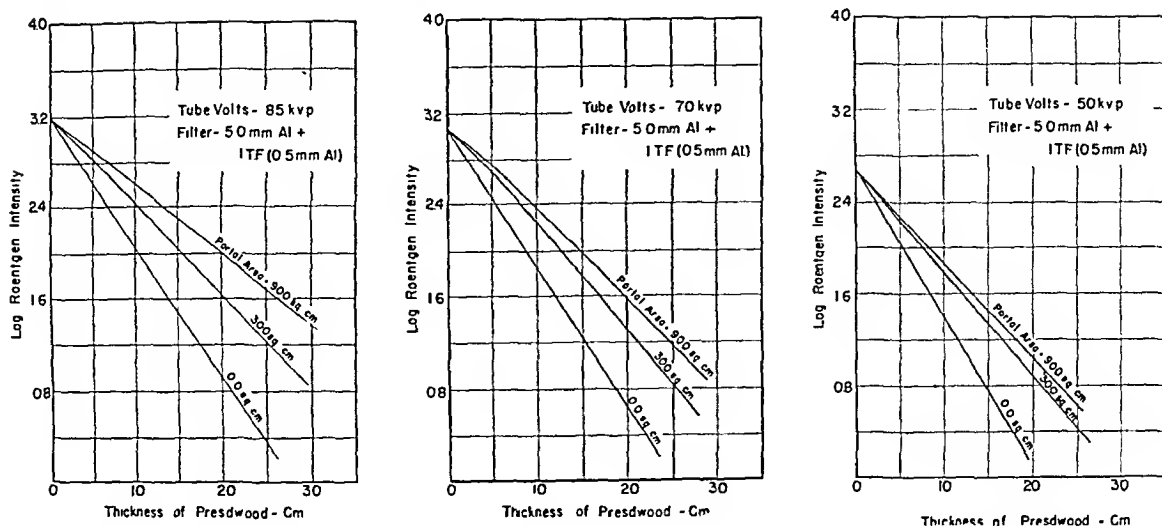


FIG. 8. Absorption curves for Masonite presdwood (density=1.07) irradiated with a four-valve, full-wave rectified generator operating at potentials of 50, 70, and 85 kv. (peak), through portals of 0.0, 300 and 900 sq. cm., with a total roentgen beam filtration of 5.5 mm. Al and with the photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed to roentgen rays directly.

DISCUSSION

It was shown in equation (20) that the contrast of a roentgenographic or roentgenoscopic image is proportional to the image's roentgen-ray intensity distribution function usually given by equation (11) or (13). It is therefore possible with the data which have just been presented to evaluate the manner in which contrast is affected by various roentgen conditions. Thus if F_1 and F_2 are the intensity distribution functions for two different circumstances, the percentage change in contrast which occurs when one progresses from one condition to the other will be

$$\% \Delta C = \frac{F_2 - F_1}{F_1} \times 100. \quad (21)$$

In the following paragraphs several illustrative examples are given to demonstrate

the manner in which equation (21) may be employed.

(a) *Effect of Kilovoltage on Roentgen Contrast.* A perusal of the tables indicates that the changes in the mass absorption coefficients which occur when the kilovoltage applied to the roentgen tube is altered are

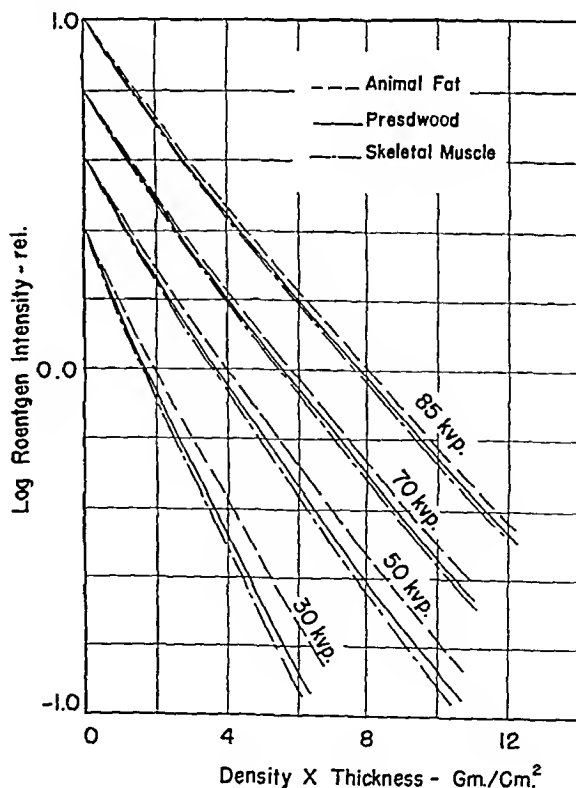


FIG. 9. Absorption curves for animal fat (density=0.92), Masonite presdwood (density=1.07) and skeletal beef muscle (density=1.05), irradiated with a four-valve, full-wave rectified generator operating at potentials of 30, 50, 70, and 85 kv. (peak), with a roentgen-ray beam filtration of 0.5 mm. Al, and with the photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed with intensifying screens. These data were obtained in the absence of scattered radiation.

TABLES VI TO IX

RATIOS OF PRIMARY TO TOTAL RADIATION RECEIVED BY ROENTGENOGRAPHIC FILMS EXPOSED WITH INTENSIFYING SCREENS AND BY ROENTGENOSCOPIC SCREENS (PATTERSON TYPE "B"). DATA INCLUDE VALUES FOR PHANTOM THICKNESSES RANGING FROM 0.0. TO 30 CM. OF MASONITE PRESWOOD (DENSITY = 1.07 CM.), FOR FOUR KILOVOLTAGES, FOR TWO PORTAL AREAS AND FOR TWO DEGREES OF FILTRATION

TABLE VI
Data applicable to conditions where:
Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al)
Portal area = 300 sq. cm.

Thickness of Preswood (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	1.000	1.000	1.000	1.000
2.5	0.740	0.755	0.770	0.805
5.0	0.620	0.635	0.650	0.690
7.5	0.530	0.550	0.565	0.615
10.0	0.455	0.475	0.500	0.560
12.5	0.385	0.415	0.445	
15.0	0.330	0.360	0.395	
17.5	0.280	0.310	0.350	
20.0	0.240	0.270	0.310	
22.5	0.205	0.235		
25.0	0.175	0.205		
27.5	0.150			
30.0	0.130			

TABLE VII
Data applicable to conditions where:
Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al)
Portal area = 900 sq. cm.

Thickness of Preswood (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	1.000	1.000	1.000	1.000
2.5	0.700	0.715	0.730	0.745
5.0	0.540	0.555	0.570	0.590
7.5	0.420	0.445	0.460	0.480
10.0	0.325	0.350	0.380	0.410
12.5	0.250	0.275	0.310	
15.0	0.195	0.220	0.255	
17.5	0.150	0.175	0.215	
20.0	0.115	0.135	0.180	
22.5	0.090	0.110		
25.0	0.070	0.087		
27.5	0.0540			
30.0	0.0415			

TABLE VIII
Data applicable to conditions where:
Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 5.0 mm. Al
Portal area = 300 sq. cm.

Thickness of Preswood (cm.)	Kilovolts (peak)		
	85	70	50
0.0	1.000	1.000	1.000
2.5	0.760	0.750	0.790
5.0	0.630	0.620	0.655
7.5	0.525	0.525	0.550
10.0	0.440	0.440	0.470
12.5	0.370	0.375	0.400
15.0	0.310	0.320	0.340
17.5	0.260	0.270	0.295
20.0	0.215	0.230	0.250
22.5	0.180	0.195	
25.0	0.155	0.165	
27.5	0.130		
30.0	0.105		

TABLE IX
Data applicable to conditions where:
Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 5.0 mm. Al.
Portal area = 900 sq. cm.

Thickness of Preswood (cm.)	Kilovolts (peak)		
	85	70	50
0.0	1.000	1.000	1.000
2.5	0.750	0.710	0.750
5.0	0.560	0.535	0.570
7.5	0.420	0.415	0.455
10.0	0.325	0.325	0.365
12.5	0.245	0.255	0.290
15.0	0.185	0.195	0.230
17.5	0.140	0.150	0.180
20.0	0.105	0.120	0.145
22.5	0.082	0.093	
25.0	0.062	0.072	
27.5	0.047		
30.0	0.037		

much greater for calcified than for non-calcified tissues. It will therefore be necessary to treat the problem in two parts.

First, let us consider an image produced by a plane of fat tissue, having a density of 0.92, which separates two muscle bundles,

TABLES X TO XIII

RATIOS OF PRIMARY TO TOTAL RADIATION RECEIVED BY ROENTGENOGRAPHIC FILMS EXPOSED WITHOUT INTENSIFYING SCREENS. DATA INCLUDE VALUES FOR RANGE OF PHANTOM THICKNESS EXTENDING FROM 0.0 TO 20 CM. OF MASONITE PRESWOOD (DENSITY = 1.07 CM.), FOR FOUR KILOVOLTAGES, FOR TWO PORTAL AREAS AND FOR TWO DEGREES OF FILTRATION

TABLE X

Data applicable to conditions where:
Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al)
Portal area = 300 sq. cm.

Thickness of Preswood (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	1.000	1.000	1.000	1.000
2.5	0.710	0.725	0.740	0.780
5.0	0.565	0.590	0.605	0.655
7.5	0.465	0.490	0.515	0.565
10.0	0.390	0.420	0.450	0.500
12.5	0.330	0.360	0.390	
15.0	0.285	0.310	0.345	
17.5	0.240	0.265	0.305	
20.0	0.205	0.230	0.270	

TABLE XI

Data applicable to conditions where:
Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al)
Portal area = 900 sq. cm.

Thickness of Preswood (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	1.000	1.000	1.000	1.000
2.5	0.675	0.690	0.700	0.740
5.0	0.480	0.500	0.525	0.580
7.5	0.365	0.390	0.425	0.480
10.0	0.275	0.310	0.350	0.400
12.5	0.210	0.245	0.290	
15.0	0.165	0.195	0.240	
17.5	0.130	0.155	0.200	
20.0	0.100	0.125	0.165	

TABLE XII

Data applicable to conditions where:
Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 5.0 mm. Al
Portal area = 300 sq. cm.

Thickness of Preswood (cm.)	Kilovolts (peak)		
	85	70	50
0.0	1.000	1.000	1.000
2.5	0.740	0.740	0.740
5.0	0.600	0.590	0.585
7.5	0.490	0.475	0.490
10.0	0.405	0.395	0.415
12.5	0.335	0.330	0.350
15.0	0.280	0.280	0.300
17.5	0.235	0.240	0.260
20.0	0.195	0.205	0.225

TABLE XIII

Data applicable to conditions where:
Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 5.0 mm. Al
Portal area = 900 sq. cm.

Thickness of Preswood (cm.)	Kilovolts (peak)		
	85	70	50
0.0	1.000	1.000	1.000
2.5	0.700	0.700	0.715
5.0	0.500	0.500	0.540
7.5	0.380	0.370	0.415
10.0	0.280	0.280	0.330
12.5	0.210	0.220	0.260
15.0	0.160	0.165	0.210
17.5	0.120	0.135	0.170
20.0	0.092	0.110	0.145

each having a density of 1.05 and a thickness of 1 cm. Let us further imagine that these tissues are located in a structure 7.5 cm. in thickness (e.g. the arm) and occupy a position several centimeters from a film which is to be exposed without intensifying screens. If the roentgen beam filtration is 0.5 mm. Al, the area to be irradiated is 300 sq. cm. and a grid is not used, it is evident

from Tables III, v and x that the intensity distribution function (equation (11)) at 70 kv. (peak) is

$$F_1 = (0.121 \times 1.02 \times 1.05 - 0.121 \times 0.96 \times 0.92)(0.490 \times 1.0) = 0.0113$$

and at 50 kv. (peak) is

$$F_2 = (0.130 \times 1.03 \times 1.05 - 0.130 \times 0.94 \times 0.92)(0.515 \times 1.0) = 0.0142.$$

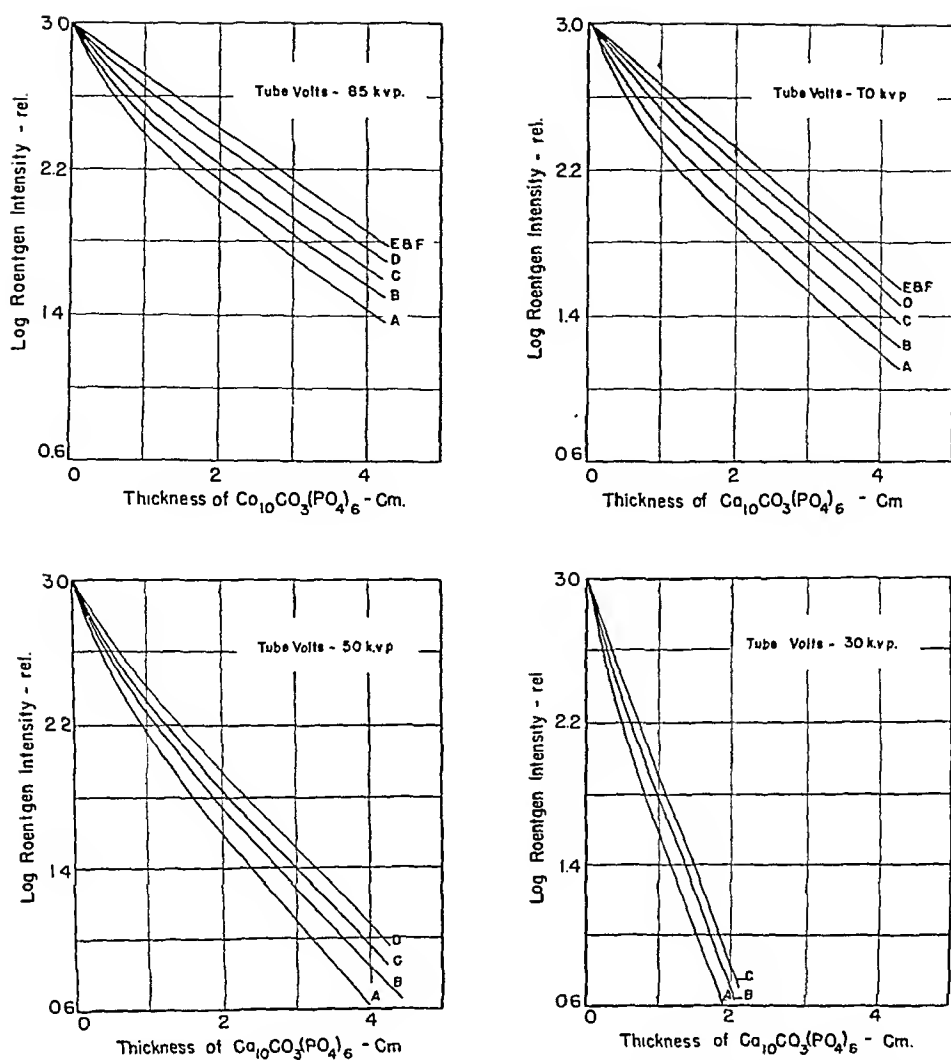


FIG. 10. Absorption curves for carbonate apatite (density=1.00) irradiated with a four-valve, full-wave rectified generator operating at potentials of 30, 50, 70 and 85 kv. (peak), with a roentgen-ray beam filtration of 0.5 mm. Al (inherent tube filtration), with a photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed with intensifying screens and with scattered radiation reaching the intensitometer effectively reduced to zero. Curves A to F refer respectively to conditions where additional filtration of 0.0 cm., 2.5 cm., 5.0 cm., 10 cm., 20 cm., and 30 cm. of Masonite presdwood (density=1.07) is present.

Therefore, from equation (21) the contrast of the image increases approximately 25 per cent between the two conditions. It may be easily shown that this change is somewhat smaller when a grid is used and when the thickness of the structure is greater than 7.5 cm.

A change in contrast of 25 per cent is relatively small and is just beyond the lower limit of perceptibility. The effect of kilovoltage on soft tissue contrast is therefore not great.

If the image were produced by a calcified structure having a density of 2.0 and a thickness of 0.25 cm. and surrounded by skeletal muscle, the intensity distribution functions at 70 and 50 kv. (peak) would be (see Tables III, V, IX, XXVIII and XXIX)

$$F_1 = (0.121 \times 1.02 \times 1.05$$

$$- 0.55 \times 2.0)(0.490 \times 0.5) = 0.117$$

and

$$F_2 = (0.130 \times 1.03 \times 1.05$$

$$- 0.70 \times 2.0)(0.515 \times 0.5) = 0.163.$$

Such a decrease in kilovoltage would therefore increase the contrast of the image by 40 per cent, an amount somewhat above the minimum level of perceptibility. In this derivation interpolated values of the mass absorption coefficient of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6$ were used.

It may seem strange to some readers that the influence of kilovoltage on contrast is not greater than that indicated in the examples just cited for there are several reports in the roentgenological literature

expressed in terms of decadic logarithms and τ and σ are the photoelectric and scattering coefficients respectively expressed in terms of Napierian logarithms. The value of the photoelectric coefficient is a function of the third power of the exposing radiation and of the fourth power of the material's atomic number whereas that of the scattering coefficient is relatively independent of both of these parameters.* Within the range of potential from 40 to 85 kv. (peak), the values of the photoelectric coefficient of

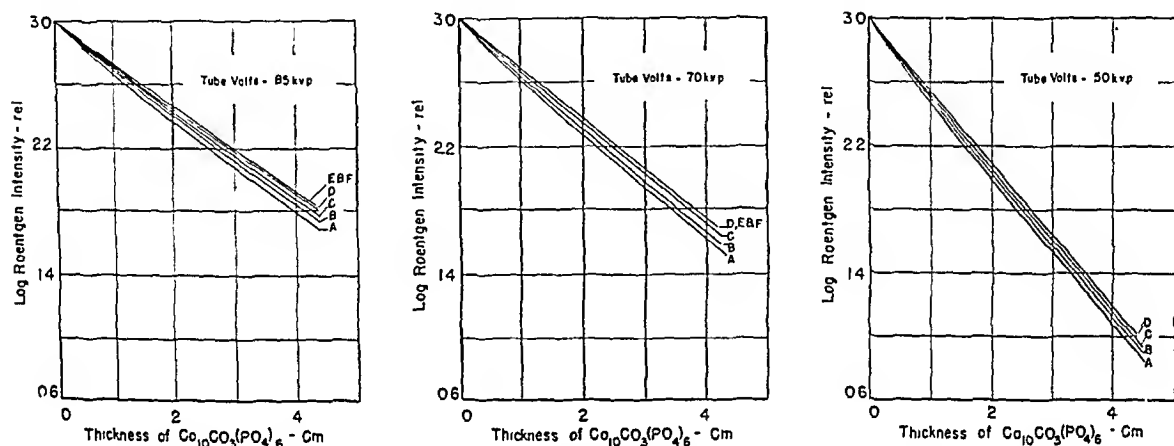


FIG. 11. Absorption curves of carbonate apatite irradiated with a four-valve, full-wave rectified generator operating at potentials of 50, 70 and 85 kv. (peak), with a total roentgen-ray beam filtration of 5.5 mm. Al, with the photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed with intensifying screens and with scattered radiation reaching the intensitometer effectively reduced to zero. The symbols A to F have the same significance as in Figure 10.

which lead one to expect a much larger effect. These views, however, are based on the belief that the value of the mass absorption coefficient of a material is a function of the third power of the wavelength of the exposing radiation and therefore of the third power of the reciprocal of the potential impressed on the roentgen tube. Abundant experimental evidence does not support the existence of such a simple relationship. Indeed, the mass absorption coefficient of a material appears to be composed of two parts, a photoelectric coefficient and a scattering coefficient, which are related according to the equation

$$2.3\mu b = \tau + \sigma \quad (22)$$

where b is the mass absorption coefficient

a material composed of elements of low atomic number such as hydrogen, carbon, nitrogen and oxygen, are small compared to those of the material's scattering coefficient. Accordingly, the values of the mass absorption coefficients of muscle, fat and other non-calcified tissues are largely unaffected by the wavelength of the exposing radiation under these conditions, and changes in roentgen tube kilovoltage therefore do not have a profound influence on contrast.

(b) *Effect of Portal Size on Contrast.* The effect of portal size on the contrast of images produced by objects separated from the film or screen by more than a few

* For a more exhaustive treatment of this subject the reader is referred to a recent communication by Victoreen.⁷

TABLES XIV-XIX

MASS ABSORPTION COEFFICIENTS EXPRESSED IN TERMS OF DECADIC LOGARITHMS OF $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6$, THE PRINCIPAL INORGANIC CONSTITUENT OF BONE. DATA ARE APPLICABLE TO CONDITIONS WHERE EXPOSURES ARE MADE WITH INTENSIFYING SCREENS

TABLE XIV

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al)

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	0.93	1.08	1.26	1.80
1.0	0.40	0.48	0.63	1.09
2.0	0.32	0.39	0.52	0.99
3.0	0.31	0.36	0.49	0.95
4.0	0.29	0.35	0.48	

* Density of material = 1.00.

TABLE XV

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 2.5 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	0.73	0.83	0.93	1.44
1.0	0.36	0.42	0.52	1.04
2.0	0.31	0.37	0.48	0.95
3.0	0.29	0.36	0.48	0.93
4.0	0.28	0.35	0.47	

* Density of material = 1.00.

TABLE XVI

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 5.0 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	0.50	0.64	0.80	1.14
1.0	0.35	0.46	0.61	0.99
2.0	0.31	0.36	0.48	0.95
3.0	0.29	0.35	0.47	
4.0	0.28	0.35	0.47	

* Density of material = 1.00.

TABLE XVII

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 10 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.41	0.50	0.69
1.0	0.32	0.38	0.52
2.0	0.29	0.36	0.48
3.0	0.28	0.35	0.47
4.0	0.28	0.35	0.47

* Density of material = 1.00.

TABLE XVIII

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 20 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)	
	85	70
0.0	0.32	0.39
1.0	0.29	0.35
2.0	0.28	0.35
3.0	0.28	0.35
4.0	0.27	0.34

* Density of material = 1.00.

TABLE XIX

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 30 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)	
	85	70
0.0	0.31	0.36
1.0	0.29	0.35
2.0	0.28	0.35
3.0	0.27	0.34
4.0	0.27	0.34

* Density of material = 1.00.

centimeters may be easily evaluated from Tables VI to XIII. For example, if one is roentgenoscopy a 20 cm. subject with a type B screen at 70 kv. (peak), the inten-

sity distribution function when a grid is not used and when the portal area is 300 sq. cm. is

$$F_1 = (b_b \rho_b - b_i \rho_i) \times 0.270 x_i.$$

TABLES XX-XXV

MASS ABSORPTION COEFFICIENTS EXPRESSED IN TERMS OF DECADIC LOGARITHMS OF $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6$, THE PRINCIPAL INORGANIC CONSTITUENT OF BONE. DATA ARE APPLICABLE TO CONDITIONS WHERE EXPOSURES ARE MADE WITH INTENSIFYING SCREENS

TABLE XX

Roentgen beam filtration = Inherent tube filtration (0.5 mm. Al) plus 5.0 mm. Al

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.39	0.46	0.57
1.0	0.32	0.39	0.50
2.0	0.28	0.34	0.46
3.0	0.27	0.33	0.46
4.0	0.26	0.33	0.46

* Density of material = 1.00.

TABLE XXI

Roentgen beam filtration = Inherent tube filtration (0.5 mm. Al) plus 5.0 mm. Al plus 2.5 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.36	0.42	0.53
1.0	0.29	0.35	0.47
2.0	0.28	0.34	0.46
3.0	0.27	0.33	0.46
4.0	0.26	0.33	0.46

* Density of material = 1.00.

TABLE XXII

Roentgen beam filtration = Inherent tube filtration (0.5 mm. Al) plus 5.0 mm. Al plus 5.0 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.35	0.39	0.50
1.0	0.28	0.34	0.47
2.0	0.27	0.33	0.46
3.0	0.26	0.33	0.46
4.0	0.26	0.32	0.46

* Density of material = 1.00.

TABLE XXIII

Roentgen beam filtration = Inherent tube filtration (0.5 mm. Al) plus 5.0 mm. Al plus 10 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.30	0.37	0.48
1.0	0.27	0.34	0.46
2.0	0.26	0.33	0.46
3.0	0.26	0.32	0.46
4.0	0.26	0.32	0.46

* Density of material = 1.00.

TABLE XXIV

Roentgen tube filtration = Inherent tube filtration (0.5 mm. Al) plus 5.0 mm. Al plus 20 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)	
	85	70
0.0	0.28	0.35
1.0	0.26	0.34
2.0	0.26	0.33
3.0	0.26	0.32
4.0	0.26	0.32

* Density of material = 1.00.

TABLE XXV

Roentgen beam filtration = Inherent tube filtration (0.5 mm. Al) plus 5.0 mm. Al plus 30 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)	
	85	70
0.0	0.27	0.34
1.0	0.26	0.33
2.0	0.26	0.32
3.0	0.26	0.32
4.0	0.26	0.32

* Density of material = 1.00.

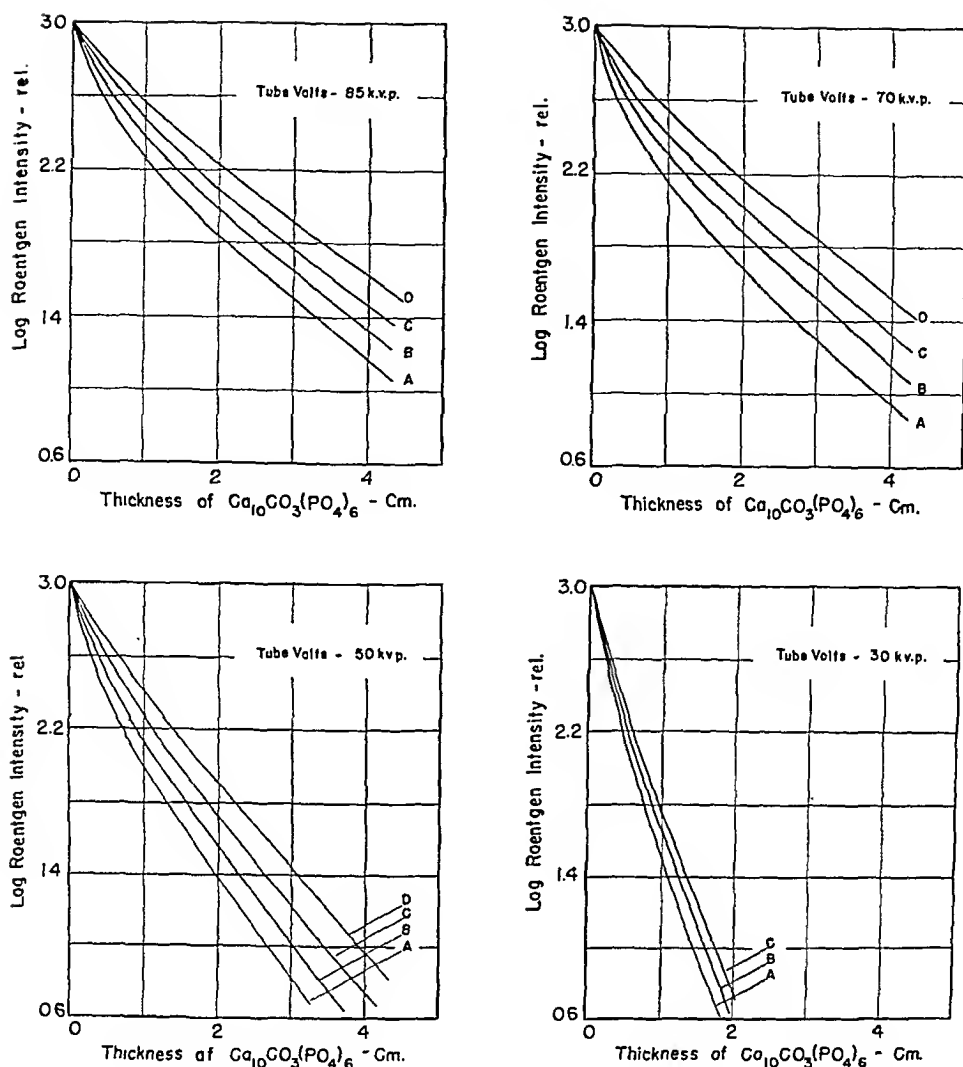


FIG. 12. Absorption curves of carbonate apatite irradiated with a four-valve, full-wave rectified generator operating at potentials of 30, 50, 70 and 85 kv. (peak), with a roentgen-ray beam filtration of 0.5 mm. Al (inherent tube filtration), with the photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed with roentgen rays directly and with scattered radiation reaching the intensitometer effectively reduced to zero. Curves A to D refer respectively to conditions where additional filtration of 0.0 cm., 2.5 cm., 5.0 cm., and 10 cm., of Masonite presdwood (density = 1.07) is present.

When the portal area is 900 sq. cm. the function is

$$F_2 = (b_b \rho_b - b_i \rho_i) \times 0.135 x_i.$$

Under this circumstance, therefore, contrast is increased 100 per cent by reducing the size of the field irradiated.

(c) *Effect of a Grid on Contrast.* In this example let us compare the contrast, obtained in a photofluorographic film when a grid having an efficiency of 80 per cent is used, with the contrast which occurs when the grid is absent.

In the derivation let us assume a subject, 20 cm. in thickness, a roentgen tube potential of 85 kv. (peak), a type D fluorescent screen and a filtration of 0.5 mm. Al. Chamberlain¹ has pointed out that the chest of a 20 cm. subject has approximately the same absorption as 10 cm. of presdwood. Therefore, from Table XI the intensity distribution function when a grid is employed is

$$F_1 = \frac{(b_b \rho_b - b_i \rho_i) \times 0.275 x_i}{1 + 0.8(0.275 - 1.000)} \\ = (b_b \rho_b - b_i \rho_i) \times 0.655 x_i$$

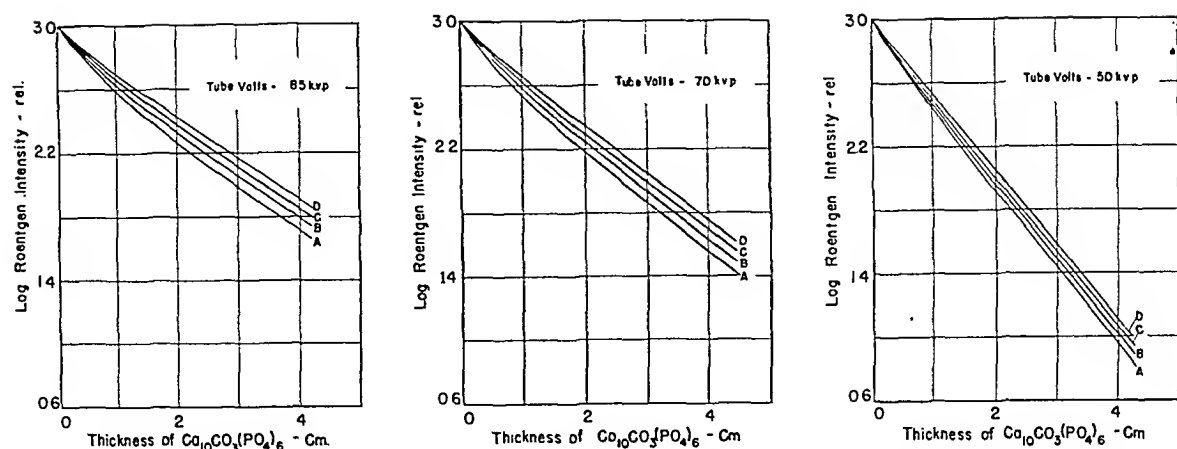


FIG. 13. Absorption curves of carbonate apatite irradiated with a four-valve, full-wave rectified roentgen generator operating at potentials of 50, 70 and 85 kv. (peak), with a total roentgen-ray beam filtration of 5.5 mm. Al, with the photoelectric intensitometer adjusted to have a spectral response similar to that of films exposed with roentgen rays directly, and with scattered radiation reaching the intensitometer effectively reduced to zero. The symbols *A* to *D* have the same significance as in Figure 12.

TABLES XXVI-XXIX

MASS ABSORPTION COEFFICIENTS EXPRESSED IN TERMS OF DECADIC LOGARITHMS OF $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6$, THE PRINCIPAL INORGANIC CONSTITUENT OF BONE. DATA ARE APPLICABLE TO CONDITIONS WHERE EXPOSURES ARE MADE WITHOUT INTENSIFYING SCREENS

TABLE XXVI

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al)

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	1.20	1.40	1.60	1.94
1.0	0.50	0.60	0.73	1.09
2.0	0.34	0.40	0.55	0.99
3.0	0.32	0.36	0.50	0.95
4.0	0.31	0.35	0.49	

* Density of material = 1.00.

TABLE XXVII

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 2.5 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	0.88	0.99	1.15	1.67
1.0	0.44	0.50	0.59	1.05
2.0	0.34	0.38	0.53	0.95
3.0	0.32	0.36	0.50	0.93
4.0	0.31	0.35	0.49	

* Density of material = 1.00.

TABLE XXVIII

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 5.0 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)			
	85	70	50	30
0.0	0.62	0.74	0.90	1.22
1.0	0.42	0.50	0.62	0.99
2.0	0.33	0.38	0.51	0.95
3.0	0.31	0.36	0.49	
4.0	0.30	0.35	0.48	

* Density of material = 1.00.

TABLE XXIX

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 10 cm. Masonite presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.47	0.55	0.75
1.0	0.34	0.39	0.55
2.0	0.31	0.36	0.49
3.0	0.30	0.35	0.48
4.0	0.29	0.35	0.48

* Density of material = 1.00.

TABLES XXX-XXXIII

MASS ABSORPTION COEFFICIENTS EXPRESSED IN TERMS OF DECADIC LOGARITHMS OF $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6$, THE PRINCIPAL INORGANIC CONSTITUENT OF BONE. DATA ARE APPLICABLE TO CONDITIONS WHERE EXPOSURES ARE MADE WITHOUT INTENSIFYING SCREENS

TABLE XXX

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 5.0 mm. Al

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.49	0.57	0.71
1.0	0.33	0.40	0.50
2.0	0.28	0.34	0.47
3.0	0.27	0.33	0.46
4.0	0.26	0.33	0.46

* Density of material = 1.00.

TABLE XXXI

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 5.0 mm. Al plus 2.5 cm. Masonite
presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.44	0.52	0.66
1.0	0.33	0.38	0.48
2.0	0.28	0.34	0.46
3.0	0.27	0.33	0.46
4.0	0.26	0.33	0.46

* Density of material = 1.00.

TABLE XXXII

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 5.0 mm. Al plus 5.0 cm. Masonite
presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.40	0.44	0.57
1.0	0.30	0.34	0.48
2.0	0.27	0.33	0.46
3.0	0.26	0.33	0.46
4.0	0.26	0.33	0.46

* Density of material = 1.00.

TABLE XXXIII

Roentgen beam filtration = Inherent tube filtration
(0.5 mm. Al) plus 5.0 mm. Al plus 10 cm. Masonite
presdwood

Thickness of $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6^*$ (cm.)	Kilovolts (peak)		
	85	70	50
0.0	0.33	0.39	0.51
1.0	0.28	0.34	0.46
2.0	0.27	0.33	0.46
3.0	0.26	0.32	0.46
4.0	0.26	0.32	0.46

* Density of material = 1.00.

and when a grid is absent

$$F_2 = (b_b \rho_b - b_i \rho_i) \times 0.275 x_i.$$

Thus the use of a grid increases photofluorographic contrast by almost 130 per cent.

(d) *Effect of Filtration on Contrast.* The effect of filtration on the mass absorption coefficients of presdwood and $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6$ depends in a large measure on the thickness of the phantom under examination, being quite marked when the thickness is small and rather insignificant when the thickness is large. The manner in which contrast is governed by filtration will therefore be very different under the two conditions.

Let us first consider the image contrast produced by a calcified object having a density of 2.0 and a thickness of 0.25 cm. when surrounded by skeletal muscle having a density of 1.05 and a thickness of 10 cm. If the field irradiated is 300 sq. cm., the roentgen beam filtration is 0.5 mm. Al, the roentgen tube potential is 70 kv. (peak) and a grid having an efficiency of 80 per cent is used, the intensity distribution function of the image when recorded by a film exposed with intensifying screens is

$$F_1 = \frac{(0.113 \times 1.02 \times 1.05 - 0.50 \times 2.0) 0.25 \times 0.475}{(1 + 0.8(0.475 - 1.000))} = 0.24.$$

When the filtration is 5.5 mm. Al the function is

$$F_2 = \frac{(0.107 \times 1.02 \times 1.05 - 0.37 \times 2.0) 0.25 \times 0.350}{1 + 0.8(0.350 - 1.000)} \\ = 0.11.$$

Thus the introduction of filtration reduces the contrast of the image by almost 55 per cent.

If, however, the calcified object is surrounded by muscle tissue having a thickness of 20 cm. and the size of the field irradiated is 900 sq. cm., the intensity distribution function of the object's image when the roentgen beam filtration is 0.5 mm. Al will be

$$F_1 = \frac{(0.109 \times 1.02 \times 1.05 - 0.39 \times 2.0) 0.25 \times 0.135}{(1 + 0.8(0.135 - 1.000))} \\ = 0.072$$

and when the filtration is 5.5 mm. Al,

$$F_2 = \frac{(0.107 \times 1.02 \times 1.05 - 0.35 \times 2.0) 0.25 \times 0.120}{(1 + 0.8(0.120 - 1.000))} \\ = 0.058.$$

Under this second circumstance the contrast of the image is reduced by the relatively insignificant amount of 19 per cent by the added filtration.

In all of the foregoing examples it has been assumed that the scattered radiation produced by Masonite presdwood is identical to that developed by comparable thicknesses of human tissue. In view of the similarity in the absorption characteristics of presdwood, fat and skeletal muscle this

assumption seems justified, although its validity will require checking by further experimentation.

It is hoped that the information which has been presented in this communication will constitute a useful guide to those who wish quantitative knowledge of the manner in which the contrast of a roentgen image is influenced by various technical factors. The data which have been given are far from complete, but additions may be expected when further investigations are completed. Meanwhile many roentgen technical problems may find ready solution from the values listed in the several tables and graphs.

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EDITORIALS

THE SIGNIFICANCE OF THE VOLUME DOSE

DURING the course of irradiation of a given lesion by means of roentgen or radium rays a certain amount of the dose administered is absorbed throughout the entire body. This fact was recognized from the earliest days of radiation therapy and references to it repeatedly appeared in the literature. However, due to lack of measuring devices, the magnitude of the dose absorbed beyond the limits of the treated area could not be exactly determined. It is not surprising, therefore, that the clinical interpretation of the effect of such a dose on the various physicochemical reactions of the body, especially in relation to radiation sickness, should have lead to considerable argumentation and speculation.

In 1935 it occurred to Ellis⁶ that some advantage may be derived from trying to express the dose absorbed beyond the treated area in some sort of a unit that could be measured at least approximately. He coined the term "volume dose" although the same term was used, in a more general sense, by Wintz earlier, and described it as so many roentgens per cubic centimeter of body tissue or "roentgen cc."

In 1940 Mayneord,¹ after a series of experimental and theoretical investigations, placed the subject on a more solid physical foundation. He suggested the term "integral dose" and introduced as a basic unit the gram-roentgen which is the energy conversion when 1 r is delivered to 1 gram of air. A megagram-roentgen (1 million gram-roentgens) is approximately equivalent to 2 calories. In radium therapy results are expressed in gram-roentgens per milligram-hour. Although this unit of Mayneord, in assuming unity density of the patient, refers to weight rather than volume, it has distinct clinical advantages. It makes, above all, possible the expression

of the total dose absorbed by the body during the course of irradiation in a manner comparable with the absorption of a gram of drug per body weight.

Following the initial work of Ellis and of Mayneord, other notable publications made their appearance in rapid succession. They dealt with the various phases of the problem by using several comparative methods of investigation. Clinical interpretations and practical evaluation of the physical data made available were likewise not slow in forthcoming.

It is, therefore, very fortunate indeed that the British Institute of Radiology, at one of its general meetings has arranged a symposium² aiming to co-ordinate the latest views on the physical, biochemical, and therapeutic aspects of the volume dose.

In this symposium, Clarkson³ discussed the results of the physical measurements made in conjunction with Mayneord on a "wax" patient. A model of elliptical cross-section and divided into slabs was constructed. In some of these slabs condenser ionization chambers were housed and measurements made for various locations. The investigations included whole body irradiation, in which the tube was placed at a distance of 250 cm. to cover the entire model, and limited field irradiations. By taking the average doses and making use of a simple calculation devised by Mayneord, tables were drawn up for whole body and different kinds of trunk irradiations. The volume dose is then found by reading the average dose from these tables and multiplying it by the weight of the patient and the surface dose.

Boag,⁴ on the other hand, presented the results of the physical measurements made in conjunction with Walter on a "celluloid" patient devised by Grimmett. This model

was constructed of cellulose acetate plates 6 mm. thick, spaced apart by washers of the same material 2 mm. thick. The plates were graphited to make them electrically conductive. Alternate plates were connected together with wires which were led to opposite poles of a battery. A sensitive galvanometer in the circuit measured the total ionization current collected from the air gaps when these were in a radiation field. As may be seen, such a model lends itself particularly to the measurement of the volume dose emanating from the irradiation of limited fields of the entire body. In this respect it is complementary to the "wax" patient which permits only whole body or trunk measurements.

Boag studied a number of situations with roentgen rays of 2 to 4 mm. Cu half-value layer, and found that the volume dose depends principally on the size of area and the site of the field and to a much lesser extent on the focal skin distance, linear dimensions of the patient and, within the ranges mentioned, on the half-value layer of the radiation.

The biochemical aspect of the volume dose is as yet unexplored, although, according to Holmes,⁵ the data available in a few cases allow rather clear suggestions for future work. The liberation of histamine and the behavior of purines following irradiation may prove of some significance. It was noted with considerable interest that uric acid, which is the end product of purine metabolism, appeared in animal tumor cells in increasing amounts twenty-four hours after irradiation.

A great deal more is known, however, about the clinical aspect of the volume dose. Ellis⁶ by reviewing the literature and collecting all the pertinent material on the subject was able to formulate rather definite conclusions as to its value in practical radiation therapy.

Ellis paid special attention to the relationship of the volume dose and a given tumor dose. The aim in clinical therapy is to administer the maximum amount of radiation to a tumor by producing the minimum possible effect on the surrounding struc-

tures or the body as a whole. Therefore, any procedure that can bring about this desideratum is worthy of consideration. Ellis found that a knowledge of the physical factors permits the advantageous adjustment of the relationship between volume dose and tumor dose in several ways. First, there is an almost proportional dependence of the volume dose on the size of the irradiated field. This means that, other things being equal, it is desirable to irradiate with fields as small as possible under the circumstances in order to keep the volume dose to a minimum value. Second, there is an inverse ratio between the volume dose and the skin target distance. This, in turn, means that to deliver the same tumor dose, other things being equal, the greater the skin target distance, the smaller the volume dose and thus the less the untoward effect from which the patient will suffer. Third, there is a definite dependence of the volume dose on the quality of the irradiating beam. Within the ranges of 2 to 4 mm. Cu half-value layer studied by Boag the difference was rather small. But in comparing 200 kv. radiation with 1,000 kv. radiation Phillips⁷ found that the volume dose is greater with the higher voltage beam for the same surface dose, other things remaining equal, although it is possible by adjusting the size and number of fields, to gain an advantage with the 1,000 kv. over the 200 kv. radiation. Fourth, the volume dose can be brought to a minimum in a given case by a proper selection of the number of fields and their efficient arrangement, other things being equal. This phase of the problem was studied in extenso by Ungar.⁸ He chose various set-ups for treatment of the same lesion and determined the relation of the "economy quotient" to the volume dose. The economy quotient was defined as the ratio of the minimum tumor dose divided by the difference between the maximum and minimum tumor doses. It was found that, other things being equal, the set-up which gave the greater economy quotient gave the smaller volume dose. From this Ungar devised a number of practical set-ups which he considered op-

timum for certain lesions under well determined circumstances.

However exacting and precise these physical considerations may be, the evaluation of the biologic phenomena directly attributable to the effect of the volume dose constitutes a most difficult problem. As Ellis so vividly states, human beings, unlike Mayneord's or Grimmer's creations, are complex physicochemical factories subject to mental and a multitude of pathologic influences acting in different individuals in very different ways. Therefore, any simple correlation of physical factors and clinical reactions appears practically impossible.

Broadly speaking, the biologic phenomena produced by the volume dose are general as distinct from local reactions which are the result of direct irradiation. According to Ellis, they may be divided into subjective and objective. The former include malaise, nausea, vomiting, headache, etc., all of which are impossible to measure or properly evaluate beyond the rough estimation that a larger volume dose is more apt to make a person ill than a smaller dose. To the latter belong the change in the blood pattern and some other changes, as for example those observed in the corpuscular volume, color index, sedimentation rate and blood pressure. The greatest hope was placed on the study of the blood pattern changes. Bush⁹ in 1943 published a curve expressing the proportional decrease of the lymphocytes in percentage of the initial count with the increase of the volume dose. Other investigators published similar curves for all types of leukocytes. However, Ellis, in examining the blood counts in a series of patients with the same view in mind, failed to find such a close correlation between the lymphocytes and still less between the other types of leukocytes and the volume dose. The same may be said of the other measurable quantities mentioned above.

The following conclusions may therefore be derived as to the significance of the volume dose in present day therapy. The physical considerations are based on sound principles and the procedures are accurate.

They aid considerably in devising methods of practical application of the roentgen and radium rays, which enable us to deliver a certain dose with greatest efficiency to the lesion, and least untoward effect to the patient. They also help in outlining methods of protection. For example, Clarkson demonstrated that a person working in a deep roentgen therapy department may absorb a volume dose which is five times as large for an equal measured stray radiation dose as that absorbed by a person engaged in roentgen diagnosis. But the volume dose is a disappointing and unreliable guide of the biologic effects. Ellis states that even if the lymphocyte curve could be correlated with the volume dose it is safer to trust the lymphocyte count rather than the physical magnitude of the volume dose in deciding when to stop treatment.

It is possible that the future will hold greater promise. In the megavoltage roentgen therapy domain where the depth doses often represent multiple values of the surface dose, the volume dose may acquire noteworthy significance. Likewise, in the therapeutic application of artificial radioactive substances the volume dose may prove a convenient indicator of the maximum tolerance under well determined circumstances.

T. LEUCUTIA

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WALTER BRADFORD CANNON
1871-1945

DR. WALTER BRADFORD CANNON, an honorary member of the American Roentgen Ray Society since 1913, died on October 1, 1945.

In 1932 the Harvard University Press published a small volume entitled "Walter Bradford Cannon: Exercises Celebrating Twenty-five Years as George Higginson Professor of Physiology. October 15, 1931."

In addition to the lengthy list of honors, publications to date, and a reproduction of the portrait accepted for the University by President Lowell, this book records the tributes paid to Dr. Cannon by Alvarez, Edsall, Lusk, and Howell. In his response, Dr. Cannon expressed some ideas which have been expanded in "The Way of an Investigator," his autobiography which is

obtainable today even in book-stores for the laity.

It was my good fortune to have "The Mechanical Factors of Digestion," then only two years published, assigned to me in 1913 to summarize for the student seminars which Dr. Sutherland Simpson exacted of his freshman medical students in physiology. It was my belief that because of the lead protection about the tube employed very early in his researches, Cannon had been spared the injuries of the other roentgen-ray pioneers. In the words of Cannon's classmate, Percy Brown, "nothing could be farther from the truth." In *Science* for November 9, 1945, Dr. Cecil K. Drinker states: "Fifteen years ago, Dr. Cannon learned he was afflicted by one of the inexorable lymphomatous diseases, all so poorly understood and all so disastrous. His illness inevitably ate a little into his humor and his irrepressible good spirits, but not into his will to work, and only those nearest to him could realize a vestige of change." It is certainly not apparent to the uninitiated reader of the Harvard 1932 volume that even as Cannon's colleague Lusk was wishing him continued health to carry on his work, Cannon knew that he was a victim of lymphoma.

If in this obituary, coming from one who from his first year in medicine on has deeply appreciated Cannon's position as Titan among physiologists, little is said of Cannon the man and much is said of his last illness, it is for a reason. Cannon's biography is on record in the references cited, and his position is such, as the founder of the art of gastrointestinal roentgen examination, that every radiologist owes it to himself and to his work, to own and to read Cannon's autobiography. A further reference is offered, to Cannon's Caldwell Lecture published in this JOURNAL for November, 1934, prefaced by the introductory remarks that only Percy Brown can make.

But there is very little in Cannon's own writings that bears on his roentgen-ray injuries. Probably no one identified with medicine ever made more extensive personal contributions to the advancement of

knowledge, to say nothing of the thirty-one professors of physiology and allied subjects whom he had trained up to 1931. When such a life ends under circumstances that in themselves advance the knowledge of a subject still in the stage of collecting evidence, Percy Brown and I have come independently to the conclusion that the story should be told. This is the sequence of events: In the autumn of 1896, Professor Henry P. Bowditch suggested to Cannon that he might utilize the newly discovered roentgen ray to study the process of digestion in animals. The very beginning of gastrointestinal roentgen diagnosis was when Cannon fed a bolus of mush mixed with bismuth to a goose, and watched its progress down the esophagus. (Transit time, twelve seconds.) Late in December Cannon demonstrated this phenomenon to the American Physiological Society, and Graham Lusk recalled it thirty-five years later, remarking that he told the story of the demonstration to every class he taught in physiology.

In the Caldwell Lecture aforementioned, Cannon says: "Well do I recall the sage advice of Professor Henry P. Bowditch, when, in the spring of 1897, I showed him an area on my hand from which the skin, exposed repeatedly to the strange new rays, had come away in successive layers. He remarked that we were employing a quite novel agent which might have very dangerous properties and that we ought to be cautious until we learned more about its nature. At the time I was an eager first-year medical student, not pleased with being checked in my purposes. In order to avoid further harm I surrounded the tube with a metal box, leaving a small aperture at the top through which the rays could pass. . . . Consequently today [1934] only a few scars remain, although during a decade, I often sat for hours together watching with the fluoroscope the processes of digestion in different parts of the alimentary canal."

After the tube was enclosed with lead except for a small aperture, Cannon worked so long with fluoroscopy that even scattered radiation must needs add up. Dr. Merrill C.

Sosman has written me as follows: "Dr. Cannon had rather severe, very painful x-ray burns on the ulnar side of each hand and wrist, extending onto the fifth finger, obviously acquired while holding the fluoroscopic screen with his hands on edge. These required several excisions and skin grafts and they bothered him for years, up to the time of his death. Not many men knew this and he never complained publicly; but I thought you should know it. For about fifteen years he suffered intense itching from leukemia cutis (mycosis fungoides), relieved only by roentgen treatments, and his death was eventually due to malignant lymphoma, not leukemia as reported in the *Journal of the American Medical Association*. He was one of the most beloved of the Harvard faculty, a friend and adviser to all of us, and we shall miss him sadly."

Percy Brown writes: "Walter suffered much injury as a result of his early work. I remember well the occurrences of acute dermatitis along the inside of each thigh (in much of his work his tube-container was suspended practically between his legs). This was many years ago, but more recently, in fact but a very few years before his death, he underwent an operation for the excision of an epitheliomatous lesion of his lip, from which he had gotten, apparently, good surgical results.

"Walter and I were class-mates, and I have followed the course of his life with the interest born of devoted friendship. I saw him last during the month of July, when we were both in the Massachusetts General Hospital, I for an amputation, and he for an acute exacerbation of leukemia cutis, with its intolerable itching, and its purpuric manifestations. His suffering for some time had been intense, especially since the weather was frightfully hot. I was conveyed in my wheel-chair to his room, and I marvelled at the degree of his fortitude and patience. He remained in the hospital a short time after my discharge, and was then transferred to his summer home in New Hampshire, whence I received letters from him. He knew, of course, the inevita-

ble prognosis of his case, and faced the outcome with his characteristic courage."

Cannon entered Harvard University with one hundred and eighty dollars. He earned his way through the University and the Medical School, and emerged with an earned balance of seven hundred dollars. On June 25, 1901, he was married to Miss Cornelia James, who as an author is mentioned in her own right in *Who's Who in America*. This most happy marriage was blessed with a son, Bradford, and four daughters, Wilma Denio, Linda, Marian, and Helen. Cannon found great joy in his children. When urged to work a little less hard, he took up sculpture, and modeled a head of his daughter, which took a blue ribbon in an exhibition of physician-artists. Drinker observes, "He was better than a good sculptor." Of all the honors which Cannon received, he remarked that none ever gave him more satisfaction than the "eight inches of blue ribbon" awarded to this creation. Certainly he could not have been less gratified by A. J. Carlson's review of "The Way of an Investigator," which, appearing in *The Scientific Monthly* for October, 1945, he did not live to see in print. The italics are Carlson's: "These chapters should be *must-reading for all medical students* if not all students in science in college and high school. This volume is not above the comprehension of laymen, and wide reading of Dr. Cannon's story would broaden the base of real understanding of science in our beloved land."

To resume the letter from Percy Brown: "Since his death, Cornelia has written me: 'Dear Percy, Your sweet letter comforted me. It is a strength to feel the friends gather close. Walter, like you, proved to be a martyr to the work with the x-rays. Two weeks before he died, he gave a very fine address before the Shock Committee. Then he had a normal week when we both felt he was on the road to health, when his dread disease overtook him, and after a week more or less, of coma, he died peacefully'."

RAMSAY SPILLMAN

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY

Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Sept. 17-20, 1946.

AMERICAN COLLEGE OF RADIOLOGY

Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION

Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio. Annual meeting: San Francisco, Calif., July 1-5, 1946.

ARKANSAS RADIOLOGICAL SOCIETY

Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

RADIOLOGICAL SOCIETY OF NORTH AMERICA

Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1946, to be announced.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY

Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION

Secretary, Dr. Gordon G. King, 3700 California St., San Francisco 18, Calif.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY

Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY

Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL ASSOCIATION

Secretary, Dr. Roy W. Johnson, 1407 S. Hope St., Los Angeles, Calif. Meets on second Wednesday of each month at the County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION

Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY

Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N. Y. Meets monthly on fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY

Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

CHICAGO ROENTGEN SOCIETY

Secretary, Dr. F. H. Squire, 1754 W. Congress St., Chicago 12, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY

Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY

Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

DALLAS-FORT WORTH ROENTGEN STUDY CLUB

Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meetings held in Dallas on odd months and in Fort Worth on even months, on third Monday, at 7:30 P.M.

DENVER RADIOLOGICAL CLUB

Secretary, Dr. A. Page Jackson, Jr., 1612 Tremont Place, Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY

Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA RADIOLOGICAL SOCIETY

Secretary, Dr. J. F. Pitman, Blanch Hotel Annex, Lake City, Fla. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY

Secretary, Dr. James J. Clark, 478 Peachtree St., Atlanta, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

RADIOLOGICAL SOCIETY OF KANSAS CITY

Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

ILLINOIS RADIOLOGICAL SOCIETY

Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY

Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meets annually second Sunday in May.

IOWA X-RAY CLUB

Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

KENTUCKY RADIOLOGICAL SOCIETY

Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

LONG ISLAND RADIOLOGICAL SOCIETY

Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

LOUISIANA RADIOLOGICAL SOCIETY

Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS

Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

MILWAUKEE ROENTGEN RAY SOCIETY

Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY

Secretary, Dr. Annette T. Stenstrom, 1218 Medical Arts Bldg., Minneapolis, Minn. One meeting a year at time of Minnesota State Medical Association.

NEBRASKA RADIOLOGICAL SOCIETY

Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY

Secretary, Dr. Richard C. Batt, Berlin, N. H. Four meetings a year.

RADIOLOGICAL SOCIETY OF NEW JERSEY

Secretary, Dr. H. R. Brindle, 501 Grand Ave., Asbury Pk. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

NEW YORK ROENTGEN SOCIETY

Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY

Secretary, Dr. Major Fleming, Rocky Mount, N. C. An-

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

nual meeting at time and place of State Medical Society.
Mid-year scientific meeting at place designated.

NORTH DAKOTA RADIOLOGICAL SOCIETY

Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo.
Meetings held by announcement.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY

Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse.
Three meetings a year, January, May, November.

OHIO RADIOLOGICAL SOCIETY

Secretary, Dr. Henry Snow, 1061 Reibold Bldg., Dayton, Ohio. Meets during annual meeting of Ohio State Medical Association.

PACIFIC ROENTGEN SOCIETY

Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY

Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport.

PHILADELPHIA ROENTGEN RAY SOCIETY

Secretary, Dr. C. L. Stewart, Jefferson Hospital, Meetings first Thursday of each month, October to May, at 8:00 P.M., in Thomson Hall, College of Physicians, 21 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY

Secretary, Dr. L. M. J. Freedman, 4800 Friendship Ave. Meets 6:30 P.M. at The Ruskin on second Wednesday, each month, October to May inclusive.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.

Secretary, Dr. Murray P. George, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

Secretary, Dr. A. M. Popma, 220 N. First St., Boise, Idaho.

ST. LOUIS SOCIETY OF RADIOLOGISTS

Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.

SAN DIEGO ROENTGEN SOCIETY

Secretary, Dr. Henry L. Jaffe, Naval Hospital, Balboa Park, San Diego, Calif. Meets monthly on first Wednesday at dinner.

SAN FRANCISCO RADIOLOGICAL SOCIETY

Secretary, Dr. Carlton L. Ould, University of California Hospital, San Francisco 22. Meets monthly on the third Thursday at 7:45 P.M., first six months of the year at Lane Hall, Stanford University Hospital, and second six months at Toland Hall, University of California Hospital.

SHREVEPORT RADIOLOGICAL CLUB

Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH CAROLINA X-RAY SOCIETY

Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY

Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY

Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting, Dallas, Texas, Monday, January 14, 1946.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING

Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE

Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00-5:00 P.M., Room 301, Service Memorial Institute.

VIRGINIA RADIOLOGICAL SOCIETY

Secretary, Dr. E. L. Flanagan, 116 E. Franklin St., Richmond, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY

Secretary, Dr. Thomas Carlile, 1115 Terry St., Seattle. Meets fourth Monday each month, October through May, College Club, Seattle.

X-RAY STUDY CLUB OF SAN FRANCISCO

Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly, third Thursday evening.

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY

Medical Members' meeting held monthly on third Friday at 2:30 P.M. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)

Meets on the third Friday of each month at 4:45 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

FACULTY OF RADIOLOGISTS

Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

SECTION OF RADIOLOGY AND MEDICAL ELECTRICITY, AUSTRALASIAN MEDICAL CONGRESS

Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

RADIOLOGICAL SECTION OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION

Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

CANADIAN ASSOCIATION OF RADIOLOGISTS

Secretary, Dr. J. W. McKay, 1620 Cedar Ave., Montreal, P. Q.

SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES

Secretary, Dr. Origène Dufresne, 4120 Ontario St., East Montreal, P. Q.

SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION

Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MEDICAL ASSOCIATION

Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

SOUTH AMERICA

SOCIEDAD ARGENTINA DE RADIOLOGIA

Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

SOCIEDAD PERUANA DE RADIOLOGIA

Secretary, Dr. Victor Giannoni, Apartado, 2306, Lima, Peru. Meetings held monthly except during January, February and March, at the Asociación Médica Peruana "Daniel A. Carrión, Villalta 218, Lima.

CONTINENTAL EUROPE

SOCIEDAD ESPAÑOLA DE RADIOLOGIA Y ELECTROLOGIA

Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

SOCIÉTÉ SUISSE DE RADIOLOGIE (SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT)

Secretary for French language, Dr. Babianitz, Geneva. *Secretary* for German language, Dr. Max Hopf, Effingerstrasse 49, Bern. Meets annually in different cities.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE

Secretary, Dr. Oscar Meller, Str. Banul Măracine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, Leningrad:

USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.

Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

LENINGRAD ROENTGEN RAY SOCIETY

Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

MOSCOW ROENTGEN RAY SOCIETY

Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

SCANDINAVIAN ROENTGEN SOCIETIES

The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

WATTS HOSPITAL MEDICAL AND SURGICAL SYMPOSIUM

The Third Annual Watts Hospital Medical and Surgical Symposium will be held at the Watts Hospital, Durham, North Carolina, on Wednesday and Thursday, February 13 and 14, 1946. The following is the program to be presented:

Wednesday, February 13, 1946

- 10:30 A.M. W. R. Stanford, M.D., presiding.
Address of Welcome. Mr. Sample B. Forbus, Superintendent, Watts Hospital.
- 10:35 A.M. Greetings from the Board of Trustees of Watts Hospital, Mr. George Watts Hill, President.
- 10:45 A.M. Some Remarks on Postgraduate Medicine. W. C. Davison, M.D., Dean, Duke University Medical School, Durham, N.C.
- 11:00 A.M. F. N. Bowles, M.D., presiding.
Clinico-Pathological Conference. William B. Porter, M.D., Professor of Medicine, Medical College of Virginia, and John S. Howe, M.D., Professor of Pathology, Medical College of Virginia, Richmond, Va.
- 1:00 P.M. Luncheon, Washington Duke Hotel.
- 2:30 P.M. W. W. Vaughan, M.D., presiding.
Some Hemolytic Processes Including the Rh Factor. Lt. Col. Louis Krause, Chief of Medicine, General Hospital, Camp Butner, North Carolina.
- 3:30 P.M. The Treatment of Habitual Abortion. Norris W. Vaux, M.D., Professor of Obstetrics, Jefferson Medical College, Philadelphia, Pa.
- 6:00 P.M. Barbecue Dinner at Watts Hospital, compliments of the Hospital Administration.
- 8:00 P.M. William M. Coppridge, M.D., presiding.
Psychiatry Speaks to Democracy—About Mothers and Moms. Edward A. Strecker, Professor of Psychiatry, University of Pennsylvania Medical School, Philadelphia, Pa.
- 9:00 P.M. Diverticulitis of the Colon. Arthur M. Shipley, M.D., Professor of Sur-

gery, University of Maryland Medical School, Baltimore, Md.

Thursday, February 14, 1946

- 11:00 A.M. J. B. Bullitt, M.D., presiding.
Clinico-Pathological Conference. Henry B. Mulholland, M.D., Professor of Medicine, University of Virginia Medical School, and James R. Cash, M.D., Professor of Pathology, University of Virginia Medical School, Charlottesville, Va.
- 1:30 P.M. Luncheon, Washington Duke Hotel.
- 2:30 P.M. A. H. Powell, M.D., presiding.
The Relationship of Medical Practice to Gerontology. James E. Paullin, M.D., Professor of Medicine, Emory University Medical School, Atlanta, Ga.
- 3:30 P.M. General Features of Periarthritis Nodosa, particularly from the Standpoint of Diagnosis. Louis Hamman, M.D., Associate Professor of Medicine, Johns Hopkins Medical School, Baltimore, Md.
- 6:00 P.M. Dinner, Washington Duke Hotel.
- 8:00 P.M. Hunter Sweaney, M.D., presiding.
The Pathologic Physiology of Biliary Tract Disease. I. S. Ravdin, Professor of Surgery, University of Pennsylvania Medical School, Philadelphia, Pa.
- 8:30 P.M. The Roentgenological Aspects of Biliary Tract Disease. Eugene P. Pendergrass, M.D., Professor of Radiology, University of Pennsylvania Medical School, Philadelphia.
- 9:30 P.M. The Surgical Aspects of Gallstone Disease. I. S. Ravdin, M.D.

AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians will resume its annual meetings in 1946 and has chosen Philadelphia as the meeting place and the dates May 13 to 17 inclusive. Headquarters will be at the Philadelphia Municipal Auditorium, 34th Street below Spruce. The meeting will be conducted under the Presidency of Dr. Ernest E. Irons, Chicago, Illinois, and the General Chair-

manship of Dr. George M. Piersol, Philadelphia, Pennsylvania.

BOSTON MEDICAL HISTORY CLUB

The Boston Medical History Club held its third meeting of the season on Monday, December 10, 1945, at 8:15 P.M., at the Boston Medical Library. The meeting commemorated the centennial of the birth of Röntgen and the semicentennial of his discovery of the roentgen ray. The speaker of the evening was Dr. Merrill C. Sosman,

Clinical Professor of Radiology, Harvard Medical School. An exhibition of books was arranged by Mr. James F. Ballard, Director, Boston Medical Library.

TEXAS RADIOLOGICAL SOCIETY

The annual meeting of the Texas Radiological Society will be held on Monday, January 14, 1946, in Dallas, Texas. All of the sessions and the annual banquet on Monday evening will be held at the Baker Hotel.



DEPARTMENT OF TECHNIQUE

Department Editor: ROBERT B. TAFT, M.D., B.S., M.A., 103 Rutledge Ave.
Charleston, S. C.

AN APPARATUS FOR THE UTILIZATION OF WEAK RADON TUBES

By L. CARDENAS, E.E., and J. L. WEATHERWAX, M.A.

Philadelphia General Hospital

PHILADELPHIA, PENNSYLVANIA

THE practice of using radon tubes in radiation therapy generally results in the discarding of those tubes which have decayed to 20 millicuries or less. This is to avoid the undue lengthening of the dosage time for clinic patients.

In order to utilize these tubes for the preparation of gold seeds, a vacuum apparatus was developed at the Philadelphia General Hospital. This apparatus has been in use for approximately a year and a half and has given satisfactory service. The section as shown in Figure 1 can be constructed as a separate unit with a suitable evacuating system or can be attached to the Failla-Duane emanation plant.¹ The radon is transferred from the crusher into the gold capillary by means of the usual Toepler mercury pumping system.

The idea of crushing weak radon tubes is not original with the authors. Dr. G. Failla at Memorial Hospital, New York, in 1934 devised a special stopcock for this purpose. Its use was discontinued in 1936, owing to a number of reasons, chief of which was the necessity of glassblowing and the exposure to which the technician was subjected in turning the stopcock by hand. These difficulties are overcome in the solenoid operated crusher used at the Philadelphia General Hospital.

The crusher tube shown on the right of Figure 1 is made of a thick-walled pyrex tube to insure mechanical strength. The bottom of this tube is rounded and the up-

per end is tapered and ground to fit over a hollow plug of soda glass which in turn is sealed to the bottom of a soda glass grease stopcock. This was done to avoid the use of a graded seal since emanation plants are generally constructed of soft glass tubing. Ordinary stopcock grease is used as a lubri-

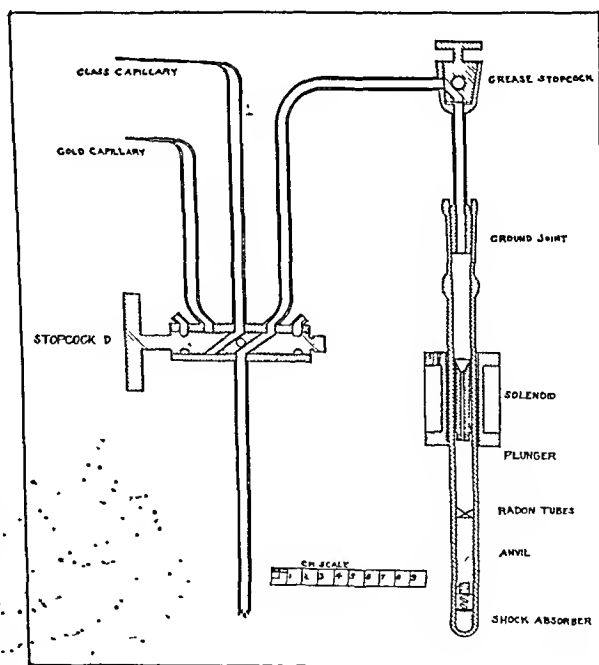


FIG. 1.

per end is tapered and ground to fit over a hollow plug of soda glass which in turn is sealed to the bottom of a soda glass grease stopcock. This was done to avoid the use of a graded seal since emanation plants are generally constructed of soft glass tubing. Ordinary stopcock grease is used as a lubri-

Failla, G. U. S. Patents 1,553,794; 1,609,614.

the upper end is flat and recessed to hold a small vertical spring. A solid brass cylinder having a flat upper surface rests on the spring. This serves as the "anvil" of the crusher. The plunger is a hollow soft iron cylinder. Its upper end is countersunk to a 60 degree angle and the bottom turned down or reduced in cross section as shown.

Figure 2 illustrates the manner in which the solenoid crusher C_5 is appended to the Failla-Duane emanation plant. Also shown in this figure is a degassing chamber C_4 used by us in an experimental investigation.

The procedure is to admit air into stopcock D and hence also into the crusher. The plug of the greased stopcock is removed and

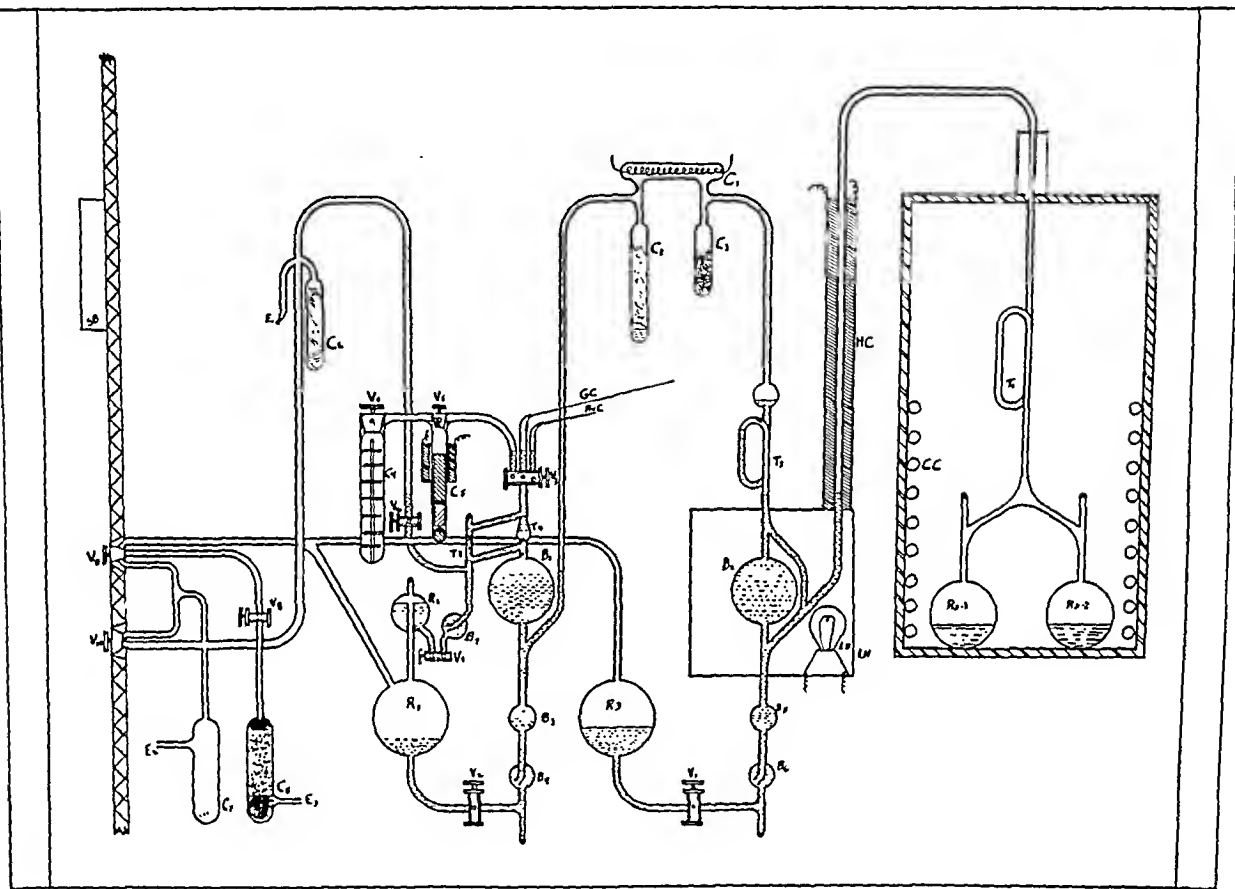


FIG. 2. Radium emanation plant, Philadelphia General Hospital; Failla-Duane type.

The lower portion of the crusher tube is enclosed in a concentric lead cylinder (not shown in the figure). This shield has a hole bored through it transversely and is illuminated from the rear. Thus the crushing of the tubes may be viewed without exposing the technician to radiation. Above the shield and also concentric with the crusher tube rests an electromagnetic coil. The entire assembly is clamped to the frame of the radon extraction apparatus to provide rigid support.

a glass funnel inserted in its place. The glass tubes which contain radon are removed from their filtration jackets and are placed in ether to remove any adherent paraffin. When they are clean and dry they are dropped through the funnel, the neck of which extends deep into the crusher. The tubes then come to rest within the hollow soft iron plunger. The funnel is removed and the plug of the greased stopcock inserted, and rotated to assure a good seal. The stopcock D and the crusher are then

evacuated. When a vacuum has been obtained the remainder of the system is isolated from stopcock *D* and the crusher. The solenoid is energized by an electrical current and the tubes fall through the hollow soft iron plunger and come to rest in an oblique position on the "anvil" as indicated in the sketch. By energizing and de-energizing the solenoid two or three times the plunger crushes the tubes to powder liberating the radon. Due to the high atomic weight of the radon and the small bore of the greased stopcock a little time should be allowed for the diffusion of the radon into the bulb of the radon apparatus directly below stopcock *D*. At the Philadelphia General Hospital it has been found that a single "stroke" will transfer 65 to 70 per cent of the radon into the gold capillary or into the glass capillary. A higher percentage of transfer is secured by taking a greater number of "strokes."

It may be found, possibly due to slight gassing of the grease or the presence of moisture or both, that the application of

one-half atmosphere of pressure will be insufficient to move the mercury up to the beginning of the gold tubing. However, by closing stopcock *D* and applying heat to the glass tube by means of a tiny gas flame the expansion of the mercury can be controlled so as to force the radon into the gold capillary.

SUMMARY

Gold seeds may be made as frequently as is desired using this apparatus without disturbing the radon supply. Furthermore the accuracy with which the proper percentage of radon can be pumped into gold seeds is increased so that it is possible to make even a small number of seeds with little error.

Since the millicurie strength of the tubes to be crushed is accurately known and since the percentage of radon transferred can be precisely determined, a collection of a small number of seeds can be made with a high degree of accuracy.

Philadelphia General Hospital
Philadelphia 4, Penna.



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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

HARTLEY, J. BLAIR, and BURNETT, C. W. F.
New light on the origin of craniolacunia. *Brit. J. Radiol.*, April, 1944, 17, 110-114.

The different theories in regard to the causation of craniolacunia are discussed and a case reported which seems to have a bearing on the subject. A child with hydrocephalus was delivered by paracentesis of the skull. There were marked lacunar changes in the anterior halves of the frontal bones at the center while the periphery and the posterior halves were normal. There was only slight abnormality in the parietal bones, which disposes of the parietal arch theory of causation. The distal portion of the squamous occipital bone derived from membrane was strikingly expanded, while the proximal segment, derived from cartilage was stunted. These findings suggest that the etiological factor was active only during the early months of ossification. It is evident that a pressure effect could not have produced this localized craniolacunia as hydrocephalus would exercise pressure equally in all directions and throughout pregnancy. An argument against the chromosomal theory of origin is furnished by the fact that craniolacunia tends to disappear with age, while chromosomal changes are never repaired. The authors conclude that this case of localized craniolacunia was caused by some dietetic defect during the earlier months of pregnancy that was remedied during the later months. Bone formed from membrane is particularly apt to be affected by such dietetic defects while bone from cartilage remains healthy. Corroborative evidence furnished by a case of fetus papyraceous is cited by the authors.—*Audrey G. Morgan.*

HARTLEY, J. BLAIR, and BURNETT, C. W. F.
Enquiry into the causation and characteristics of cephalhaematoma. *Brit. J. Radiol.*, Feb., 1944, 17, 33-41.

Very little attention has been paid in the roentgen literature to the diagnosis of cephalhematoma, though it is of considerable importance and these cases must be differentiated from craniolacunia and craniofenestria. The authors described 5 cases and give roentgenograms of them with roentgenograms of cases of craniolacunia and craniofenestria for purposes of comparison.

One factor in the causation of these cephalhematomas is birth pressure but such pressure acting on normal bones would not cause them, or they would be much more frequent. It is probable that the bone underlying the tumor is incompletely ossified. This theory is borne out by the fact that the majority of these cases occur in the children of primiparas in whom the head engages a month before birth. The tumor probably does not result from a single hemorrhage but from a series of small repeated hemorrhages. It is also probable that the fall in the prothrombin level in newborn infants is a factor in their causation. To detect their presence careful roentgen studies should be made before, during and after labor; examination of the blood of mothers and infants and detailed records of the appearance and behavior of infants at birth are also important. In treatment the author recommends the giving of a single dose of 10 mg. of vitamin K analogue (2-methyl-1:4 naphthoquinone) as soon as the lesion is discovered, as this dose prevents any appreciable fall in prothrombin concentration.—*Audrey G. Morgan.*

TINNEY, WILLIAM S., and MOERSCH, HERMAN
J. Intracranial metastasis of carcinoma of the lung. *Arch. Otolaryng.*, March, 1944, 39, 243-244.

Because of the lack of specificity of pulmonary symptoms and occasional absence of any symptoms referable to the thorax, the diagnosis of carcinoma of the bronchus not infrequently is extremely difficult. In some instances the problem is further complicated by early metastasis to the central nervous system, as exemplified by involvement of the nervous system in 52, or 12 per cent, of the 448 cases of proved carcinoma of the lung. The most interesting cases were the 19, or 4 per cent, in which the initial symptoms were referable to the nervous system. In 9 of these cases a pulmonary lesion was not suspected until a routine roentgenogram of the thorax was obtained. For this reason the authors wish to stress the importance of careful physical examination, including routine roentgenographic examination of the thorax, in every case in which an intracranial or intraspinal lesion is suspected.

It is often difficult and at times impossible to distinguish a metastatic lesion from a primary tumor of the brain or the spinal cord. The clinical manifestations in most of the patients suggested characteristically wide dissemination and rapid progression of the lesions and included a rather high incidence of personality changes. However, these clinical findings alone were not sufficiently characteristic in any case to be of much assistance in the differential diagnosis. The authors also wish to emphasize that in their series of cases the type of carcinoma of the lung was not a factor in the incidence of metastasis to the nervous system.—*Mary Frances Vastine.*

BROMLEY, J. F., WRIGHT, W. D., and SPIEGLER, G.
The eye and radiology; symposium. *Brit. J. Radiol.*, March, 1944, 17, 65-69.

Bromley discusses the physiology of the eye, comparing it to a photographic camera. The physicists use the foot candle as the unit of intensity at any given point and an alternative to this is the lumen: 1 foot candle = 1 lumen per square foot. The unit of brightness is the lambert which is the average brightness of a surface which emits or reflects 1 lumen per square centimeter. The brightness of emission of a fluorescent screen lies between the limits of 0.01 mililambert for thin persons and 0.001 mili-

lambert for thick patients or small fluoroscopic areas and therefore the amount of illumination of the screen is quite low and comes within pure rod function. The rods are distributed peripherally around the fovea centralis, 10 to 15 degrees away from it. Therefore to see clearly in a dim light the observer must look not directly at the object but 10 to 15 degrees away from it. The rods become tired very quickly so the observer should not look steadily at the object but allow his eyes to pass from one side of the object to the other, resting only for a second or two on points of special interest. This method of looking to one side of the object and using the "scanning" technique is important in training the night vision of pilots. Two other factors that affect visual acuity at night are good general condition and a sufficient oxygen supply. A sufficient amount of vitamin A is also necessary as lack of it causes deficiency of visual purple. Pilocarpine hastens the regeneration of visual purple after it has been bleached by bright light. Nicotine has a bad effect on rod vision. Alcohol does not affect the rods directly but depresses the higher interpretative centers.

Wright discusses the limitations of the eye and their effect on the interpretation of the fluoroscopic image. It is possible that brighter pictures may be obtained by the application of television principles to fluoroscopy. This would involve greater complexity and expense than the present method but the gain in brightness would probably justify it.

Spiegler discusses the roentgenogram from the physical viewpoint as a pattern of contrasts and shows by illustrations how the mind may lead to misinterpretation on the part of the eye. An improved system of interpretation will have to take into account the influence of stray radiation on contrast and definition to a greater degree than has been done in the past. An illustration is given showing the difference in opacity of the image of two pieces of lead, one placed on the front, the other on the back of the patient. The greater opacity of the image on the back is due to the fact that more scattered radiation reached this piece of lead.

The eye responds to different types of blurring (from movement, size of focal spot and graininess of screen) in different ways. The analysis of pictures of unknown non-medical objects is recommended as a useful way of training the mind in the reading of roentgenograms without being influenced by anticipations or prejudices.—*Audrey G. Morgan.*

MCLAREN, JOHN W. Bone degeneration of the temporo-mandibular joint. *Brit. J. Radiol.*, March, 1944, 17, 94-95.

Three types of bone degeneration may be demonstrated by roentgen examination of the temporomandibular joint: (1) erosion of the anterior and upper aspect of the affected condyle; (2) narrowing of the joint space with blurring of the bone outlines, indicating arthritic changes; (3) greater forward movement of the eminence of the condyle on the involved side than on the normal side.

Roentgenograms are given of a case in a man of thirty-nine who had complained of pain over the left mandibular joint and slight limitation of movement. Roentgen examination showed a circular area of degeneration on the superior aspect of the condyle of the jaw. Operation showed an area of degeneration just beneath the joint surface; the space was filled with a mucoid fluid. After the removal of this part of the condyle the patient had no further symptoms.

The condition is probably caused by trauma. This patient had been a sparring partner for fifteen years and had had repeated blows on the chin, but no serious injury at any time.—*Audrey G. Morgan.*

WINDEYER, B. W. Malignant tumours of the upper jaw. *Brit. J. Radiol.*, Jan., 1944, 17, 18-24.

Malignant tumors of the upper jaw are usually not diagnosed until late after the wall of the antrum has broken down. Valuable time is often lost in the extraction of teeth or treatment for sinusitis. The methods of diagnosis are inspection and palpation to detect swelling, softening or ulceration. Rhinoscopy may show a tumor bulging into the nose but may show only simple polypi. If polypi are small and multiple and bleed easily and if they occur in a patient past forty they suggest malignancy. Epitheliomata of the palate are often really tumors of the antrum. Transillumination may show opacity at the site of the disease. Roentgenography is of the greatest value in showing dullness of the antrum, the site and extent of destruction of the wall of the antrum and often also the outline of the tumor. It shows the extent of involvement of the ethmoids and other sinuses and extension to the base of the skull if it has occurred. Biopsy is of value in determining prognosis and methods of treatment. It must be taken from the deeper tissues and explora-

tory operation is generally necessary. To avoid increased risk of metastasis from trauma it should be performed with the diathermy electrode and the area thoroughly coagulated.

A combination of surgery and radiotherapy has proved more valuable in the treatment of these tumors than either alone. The author discusses a series of 153 cases treated by the combined method and gives roentgenograms of cases and diagrams of the method of applying radium to the antrum. Distribution of dosage is not easy to calculate because of the peculiarities in the shape of the antrum. In intracavitary radium treatment each case must be considered individually. External irradiation is first given to the whole of the affected region after the extent of the tumor has been determined. Both the 4 gm. telerradium unit and roentgen rays with a half-value layer of 2 mm. copper have been used for this purpose. Homogeneous distribution of the radiation is obtained more easily with roentgen rays and the daily sessions are shorter and therefore less troublesome for the patient. A tumor dose of from 4,500 to 5,500 r is given over a period of four to six weeks, and drainage of the antrum provided for if this has not already been done by exploratory operation. When the reaction from this treatment has subsided operation is performed. Later steps depend on the condition found at operation.

Among the 153 cases 120 were treated; the other 23, or 15 per cent, were considered too advanced or the patients refused treatment. The five year results are known only in the cases treated before 1937. Up to 1935, 69 cases were treated and 18 were symptom-free at the end of five years. In 1936 and 1937 13 cases were treated, 5 remaining free of symptoms for three years and 4 for five years. From 1936 to 1939, 30 cases were treated and of these 11 were free of symptoms after three years. These figures show a marked improvement, although all the cases seen during this period were treated. Of the 9 cases of sarcoma treated before 1937 only 1 remained free of symptoms for five years.—*Audrey G. Morgan.*

THOMPSON, CHARLES M., and GRIMES, ELMER L. Carcinoma of the nasopharynx. *Am. J. M. Sc.*, March, 1944, 207, 342-348.

This paper was written to call attention to the clinical syndrome that characterizes carcinoma of the nasopharynx. It is believed that

a lack of knowledge of this symptom complex has undoubtedly been a factor in the poor control of this highly malignant disease. Every review in the literature presents an equally discouraging percentage of cures. Many authors stress the element of late diagnosis as one of the reasons for this low percentage. The following features are associated with this disease:

(1) Cervical adenopathy. Various series taken from the literature show that this occurs in from 27.5 to 77 per cent of the cases.

(2) Nasorespiratory symptoms, as evidenced by nasal obstruction, discharge or epistaxis is reported in 30 per cent of the cases.

(3) Neurological symptoms. Paralysis of one or more cranial nerves, the most frequently involved cranial nerves are V, VI, IX, resulting in facial pain, diplopia and dysphagia, respectively. These findings plus headaches are explained by direct extension of the tumor into the middle fossa of the skull. Roentgenograms of the base of the skull show a typical melted-out appearance of the sphenoid and the petrous portion of the temporal bone. Due to involvement of the cervical sympathetic chain, a Horner's syndrome may develop.

(4) Ear symptoms. As most of the tumors arise in or near the fossa of Rosenmüller, a number of auricular manifestations may be expected as early complaints. Tinnitus and a sensation of stuffiness are the other leading complaints.

(5) Duration of symptoms. It was claimed by Furstenburg that the average duration of symptoms before diagnosis was fifteen months.

Once the diagnosis is proved, irradiation to the limit of the skin and physical tolerance is the only accepted method of treatment. The general opinion is that surgery is not indicated in the treatment of these tumors.

Schmincke pointed out that these tumors arose in a lympho-epithelial region where normally considerable lymphoid tissue abounds and that they were simply anaplastic carcinomas arising from the nasopharyngeal mucosa with many lymphocytes mixed in coincidentally. They are not malignant lymphomata.

It is pointed out that profoundly ill patients can be dramatically relieved temporarily by irradiation. In several of the authors' cases, the patients were rendered symptom free for weeks or months with complete clinical regression of the primary and also the cervical node enlargement. Subsequent recurrence of the tumor or metastases has been found to be radioresistant. Therefore, once the diagnosis has been estab-

lished, all patients should be treated to the limit of skin and physical tolerance even though clinically one can no longer find disease.—*James J. McCort.*

NECK AND CHEST

PAYNE, REGINALD T., TOD, MARGARET C., and LEDERMAN, M. Diagnosis, classification and treatment of tumours of the salivary glands; symposium. *Brit. J. Radiol.*, Jan., 1944, 17, 3-12.

In any large series of tumors those of the salivary glands constitute only 1 to 2 per cent. They are of great interest, however, as it is very difficult to determine whether they are benign or malignant. Deep roentgen treatment is now used as an aid in differential diagnosis as well as in treatment. A classification of the benign and malignant forms is given and congenital hypertrophies are also included although they are not tumors, strictly speaking. Recurrence may take place many years after operation and a patient can hardly be considered free from the danger of recurrence as long as he lives.

A combination of irradiation and surgery has been found more effective than either alone. A high percentage of five year recoveries can be brought about in this way but, as mentioned above, a five year recovery is not so decisive as in tumors in other locations. Lymphosarcomas are quite radiosensitive. The mixed tumors of the parotid which are the most frequent form are less so. The best method of treatment for these is surgery followed by implantation of radium needles. The volume of tissue irradiated plays a part in the results, and the smaller the volume the greater the tolerance. That is why the tumor should be removed surgically before irradiation, which should be given in a single course within a month of operation. The incidence of recurrence also seems to be reduced when surgery is combined with irradiation. The technique and dosage of irradiation, which must be adapted to the individual case, are discussed. When surgery is impossible or contraindicated radiotherapy with radium or roentgen rays gives good results in some cases.—*Audrey G. Morgan.*

JOHNSTONE, A. S. Salivary calculus or tartar. *Brit. J. Radiol.*, Jan., 1944, 17, 31-32.

Some confusion has arisen from the different meaning attached to the word salivary calculus by physicians and dentists. A salivary calculus

is really a concretion in one of the salivary glands or its ducts while the name tartar should be applied to surface deposits on the teeth. These may reach large size and resemble tumors. A case is described in a woman of fifty-eight who showed the changes of hypertrophic osteoarthritis. She also had a swelling of the right cheek which had been increasing in size for twenty years. An intra-oral occlusal roentgenogram showed a bone tumor apparently originating from the alveolar margin of the right maxilla. Only three teeth, the fourth, fifth and sixth, remained in the right maxilla and these were surrounded by the dense radiopaque deposit. It was removed with the three teeth which had become loosened by absorption of the alveolus. There was no evidence of invasion. The growth was diagnosed as a "salivary calculus" and removed, but without any improvement in the osteoarthritis. It was really an enormous deposit of tartar.—*Audrey G. Morgan.*

BERSACK, S. R. Carcinoma of the esophagus in association with achalasia of the cardia. *Radiology*, March, 1944, 42, 220-223.

Achalasia means a failure of the sphincter of the esophagus at the cardia to relax. It results in an accumulation of saliva and food over long periods of time that is irritating and theoretically might be supposed to bring about the development of carcinoma. Rake in fact reported an incidence of 20 per cent carcinoma in 15 cases of achalasia and Gottstein an incidence of 10 per cent in 33 cases.

But among 227 patients with carcinoma of the esophagus admitted to the Edward Hines Hospital, Hines, Ill., the carcinoma was associated with achalasia in only 1 case. The history of this case is given. This low incidence of carcinoma associated with achalasia is all the more noteworthy because shallow ulcerations, nests of epithelial hyperplasia and wart-like formations have been seen repeatedly in achalasia. Frequently small irregularities and filling defects are seen in the dilated esophagus but they may be caused by retained secretion and food particles. Roentgen examination of the esophagus should not be made until after the retained contents of the esophagus have been evacuated.

In order to show definitely any relationship between achalasia and carcinoma of the esophagus it would be necessary to prove statis-

tically that carcinoma is decidedly more frequent in cases of achalasia than in the general population of the same age group. No such statistics are available—in fact, there are no comprehensive statistics for achalasia. This group of cases would seem to argue against any connection between the two conditions.—*Audrey G. Morgan.*

SCHWARTZ, LEO. Adenoma of the trachea and the bronchus. *Arch. Otolaryng.*, March, 1944, 39, 231-242.

Statistics disclose that there is actually a predilection of primary tumors for the lungs and bronchi and that 12 to 15 per cent of all cancers originate in them. In the light of recent knowledge it is found that 5 to 10 per cent of all primary endobronchial tumors are benign.

Histological Origin of Primary Endobronchial Tumors. The adenomas probably arise from the gland cells or from the cells of the gland ducts. Originating as they do in the submucosa, they lift the mucosa over their surface as they grow; therefore, the mucosa presents itself to the endoscopist's eye as the smooth glistening surface of the tumor. As the tumor grows and the lumen of the trachea or bronchus becomes partially or totally filled with the mass, molding and encasing pressure is exerted on it by the rigid bronchial or tracheal cartilaginous frame, imparting to the tumor a rounded and elongated form.

The author wonders whether this growth in the female might not be distinct from that occurring in the male and, in fact, arise from primordial gonadal cell rests. The recurring hemoptyses that are frequently concurrent with the menses, as well as the fact that these patients frequently give a history of pulmonary bouts beginning at the menarchal period, seem to support this conjecture.

Tumor Growth and Extension. Three types are described: (1) pedunculated type which, as a rule, grows entirely within the lumen; (2) intramural type which presents a flat base and grows between the cartilaginous rings; (3) endoextrabronchial or dumbbell type in which a constriction takes place at the bronchial wall. The smaller portions present endobronchially and the large, extrabronchially.

Symptoms and Physical Signs. Adenoma presents no findings which are peculiar to itself. The findings are those characteristic of bronchial obstruction and depend on the location

of the tumor, the type of obstruction produced, the amount of tributary alveolar tissue obstructed and other factors, such as the type and the virulence of secondary infection.

Roentgenologic Manifestations of Bronchial Obstructions. These depend on the type of obstruction produced: (1) Stop valve obstruction—the bronchus is corked and the roentgenologic findings are those of atelectasis. (2) By-pass valve obstruction—air can pass in and out of the lung but only in limited amounts. The asthmatoïd wheeze can be heard at the open mouth. (3) Check valve obstruction—the occluding body interferes with either the inspiratory or the expiratory phase of respiration leaving the other phase unimpaired. The roentgenologic findings can therefore be either those of atelectasis or emphysema.

Differential Diagnosis. The lesion with which bronchial adenoma is most frequently confused is bronchogenic carcinoma. Adenoma is overwhelmingly a disease of young women. Carcinoma is preponderantly a disease of old men. Most cases of adenoma in women occur during the years of fertility. There is some evidence that adenoma at times undergoes cancerous transition. Hemoptyses occurring with adenoma are inclined to be much more profuse than those with carcinoma and are frequently encountered during the menstrual period.

Treatment. The tumors that arise from stalk-like bases and have neither mural nor extra-bronchial extensions can be entirely cured by bronchoscopic means. Those tumors which show mural and extramural extension and all cases complicated with irreparable pulmonary damage as a result of prolonged obstruction demand surgical intervention.—*Mary Frances Vastine.*

SHINALL, HAROLD L. Roentgen diagnosis of bronchiogenic carcinoma. *Radiology*, March, 1944, 42, 213-219.

About 15,000 persons die in the United States every year of bronchiogenic carcinoma. The diagnosis is very difficult, neither clinical nor roentgen signs alone being sufficiently definite to establish it. But with careful clinical examination and absolutely accurate roentgen technique diagnosis can be made in a maximum of 87 per cent of the cases from a combination of these findings.

The authors discuss 40 cases seen at the St. Louis City Hospital in the past five years in

which both roentgen and clinical examination was made. Among these the clinical examination was sufficient for diagnosis in only 6 cases, or 15 per cent, while diagnosis was made from both clinical and roentgen signs in 16, or 45 per cent.

There are three types of bronchiogenic carcinoma—those arising from the lining epithelium, those arising from the mucous glands of the submucosa and those arising from the pulmonary alveoli. Only 1 case suggesting the possibility of an alveolar origin was seen. Roentgenograms of the different types of cases in different areas of the lung are given.

The clinical features which aid in diagnosis are the age of the patient which is usually over forty years, the average in these cases being fifty eight years; the duration of the illness, three months or more; the cough usually dry and non-productive or there may be none at all; expectoration of blood at some time during the illness; loss of weight usually out of proportion to the lung involvement. There is no fever or other signs of infection unless secondary infection takes place. The chief roentgen sign is a unilateral, rounded nodular shadow, usually in the hilar region.

Fariñas holds that when a chest roentgenogram shows an expiratory emphysema, an atelectatic zone in any field, or a dense shadow in the hilar region serial bronchography is indicated for the detection of bronchiogenic carcinoma.—*Audrey G. Morgan.*

WEINSTEIN, MANDEL, and TYAU, STEVEN. Intrabronchial spread following thoracoplasty. *Am. Rev. Tuberc.*, March, 1944, 49, 238-250.

Since the advent of surgical collapse of pulmonary tuberculosis, postoperative tuberculous spread has been a serious complication. Aspiration of infectious bronchial secretions during and following operation is the prime factor concerned. In the hours immediately following operation, cough, expectoration, and respiratory, ciliary, and peristaltic movements of the bronchi are abolished or diminished. This encourages bronchial stasis, plugging of bronchopulmonary segments, and atelectasis. As might be expected, the patients with more extensive disease and more cavitory exudate are more prone to postoperative spread.

Nineteen postoperative spreads in 14 patients are reported by the authors. This tuberculous extension represents an operative incidence of approximately 10 per cent—198

thoracoplasties having been performed in the period represented by this report. Negroes develop spread twice as frequently as whites; moreover, 4 deaths, all Negroes, resulted from the spreads—a mortality of 2 per cent. Tuberculous spreads involve twice as many contralateral as homolateral lungs while bilateral extension occurred only in 4 cases. All patients with mild spreads recovered; as might be anticipated the severe spreads accounted for all postoperative fatalities.

No single or multiple procedures can always prevent tuberculous spreads, but maintaining the tracheobronchial tree free from much secretion will help by preserving open airways and precluding the movement of infected tuberculous exudate throughout the respiratory system.—*John R. Hannan.*

HAMILTON, JOSEPH G., SOLEY, MAYO H., REILLY, WILLIAM A., and EICHORN, KARL B. Radioactive iodine studies in childhood hypothyroidism. *Am. J. Dis. Child.*, Nov., 1943, 66, 495-502.

The authors employed labeled (radioactive) iodine to determine the ability of the thyroids in two groups of hypothyroid children to concentrate iodine.

They summarize their study as follows:

"The thyroids of children with hypothyroidism and without goiters are able to concentrate only small amounts of orally administered iodine, as compared with the thyroids of normal children or adults. In these hypothyroid children, the remaining thyroid tissue concentrated a larger percentage of a dose of 0.1 microgram than of a dose of 14 mg. of iodine.

"The thyroids of two children with goiters and with severe hypothyroidism took up relatively large amounts of iodine and by chemical analysis contained both thyroxin and diiodotyrosine in considerable quantities. The uptake curves of the thyroids as measured in situ were similar to those seen in hyperthyroidism in adults. Radioautographs made from sections of the thyroids of both of these children indicate that by the fifth day after the oral administration more of the iodine was in the cells than in the colloid."—*R. S. Bromer.*

GELLIS, SYDNEY S., and PETERS, MICHAEL. Mumps with pre-sternal edema. *Bull. Johns Hopkins Hosp.*, Oct., 1944, 75, 241-250.

The authors report an incidence of presternal

edema complicating epidemic parotitis in 6 per cent of 502 patients at the Station Hospital, Fort Benning, Georgia. The condition appears to be of no particular consequence since only 5 patients developed symptoms coincident with the edema—2 had dysphagia for twenty-four hours, 1 had hoarseness and 2 were tender to palpation over the sternum. All patients having this complication were afebrile at the time of onset except those who already had orchitis. The incidence of orchitis in the 30 cases of edema was no greater than in the remaining 472 cases. Roentgen studies showed no demonstrable intrathoracic changes, though the thickening of the presternal tissues was seen in the lateral roentgenograms. The edema is central, the shape of a necklace, obliterates the sternal notch and is variable in extent. In their cases it developed between the third and twelfth days of illness and lasted from two to eighteen days. They consider it due to obstruction of lymphatics by swollen salivary glands.—*Angus K. Wilson.*

HURST, ALLAN, BASSIN, SYDNEY, and LEVINE, IDA. Miliary densities associated with mitral stenosis. *Am. Rev. Tuberc.*, March, 1944, 49, 276-285.

Miliary densities associated with rheumatic mitral stenosis have received little attention in the medical literature. Recent textbooks of roentgenology state that this finding is encountered occasionally in cardiac congestion, particularly secondary to mitral stenosis, but failed to stress the not infrequent permanency of the pulmonary changes.

The authors present 5 cases of bilateral, symmetrical, diffuse, miliary, and submiliary densities associated with mitral stenosis—cases selected as representative of most of the pathological changes occurring in this condition. The 5 young men were practically asymptomatic and without auscultatory pulmonary signs when a chance roentgenogram disclosed the abnormal densities. These densities are ascribed to passive pulmonary congestion with hypertension of the lesser circuit. The vessels dilate, become engorged, and finally hypertrophy. When seen on end, these vessels are revealed as rounded densities and on horizontal section are linear. In addition, some larger, denser nodules are seen at the periphery of the lower lung fields in several cases. These are attributed to perivascular fibrosis with deposition of hemosiderin

pigment from extravasation of blood. Occasionally, numerous calcific densities (thought to be due to breakdown and subsequent healing of multiple, small, stasis infarcts attendant upon severe passive congestion) are scattered throughout the lung fields.

In spite of the obvious cardiac condition, these densities are frequently imputed to and must be differentiated from the pulmonary lesions of sarcoid, miliary tuberculosis, pneumoconiosis and lymphangitic carcinomatosis.—*John R. Hannan.*

BAER, RIDGELY W., TAUSSIG, HELEN B., and OPPENHEIMER, ELLA H. Congenital aneurysmal dilatation of the aorta associated with arachnodactyly. *Bull. Johns Hopkins Hosp.*, June, 1943, 72, 309-331.

The authors report 2 cases in which they found extraordinary aneurysmal dilatation of the ascending aorta in association with arachnodactyly. They recognize the report of Ellis that approximately one-third of patients having arachnodactyly also have congenital malformations of the heart, and refer to their own previous report of interauricular septal defects, but the condition found in these 2 cases was unique in their experience. In addition to several non-contributory congenital defects (ectopia lentis, deformities of spine, and, in Case 1, of the thoracic cage), they found dilatation of the ascending aorta and cardiac enlargement. Roentgen examination by films and barium suspension failed to give any indication of the aortic enlargement. The first patient died when fourteen years of age, after developing auricular fibrillation, and the second patient died suddenly at the age of twenty-six years, after angina-like attacks of precordial pain.

The autopsy findings in both patients were remarkably alike. The enlargement of the ascending aorta was found to be due to changes affecting the elastica and muscular components. In some places the elastic fibers were frayed, in others condensed and in still others were totally absent. The muscle bundles, instead of the normal parallel distributions were irregularly branched, rarefied and between the branches there were large cystic spaces filled with a blue-staining coagulum. The medium was still further distorted by numerous irregular blood channels. There were small foci of lymphocytes in the adventitia but the authors felt they were not indicative of in-

flammatory process. There was no cellular exudate in the medium, nor was there any evidence of necrosis or degeneration.

After discussing Erdheim's "medial necrosis idiopathica cystica," which is considered due to necrosis and senile degeneration they conclude that in their cases the aneurysmal dilatation of the ascending aorta is a congenital anomaly due to abnormal development of the elastic and muscular layers. The cystic spaces filled with mucoid material are normally present in the fetus up to about three months, thereafter gradually disappearing.

The article is well illustrated with reproductions of roentgenograms, in posteroanterior projections, in support of the observation that the dilatation of the ascending aorta was not demonstrable, by excellent photographs of gross specimens and photomicrographs.—*Angus K. Wilson.*

FREEDMAN, PAUL, LEVINE, SAMUEL, and SOLIS-COHEN, LEON. Hemothorax in blood dyscrasias. *Am. J. M. Sc.*, May, 1943, 205, 692-696.

The authors report 2 cases of hemothorax which were admitted to the Jewish Hospital in a period of two months. Both occurred in males, one due to hemophilia and one due to thrombocytopenic purpura. Both patients were in the third decade of life. They are classified as non-traumatic hemothorax. In neither was it a primary manifestation of the disease. In the hemophiliac it was acute in clinical onset, while in the purpuric it was more insidious. The patient with hemophilia eventually recovered; the patient with purpura succumbed to infection in the form of an empyema. It was thought that this infection was secondary to thoracenteses and the danger of this complication is emphasized.

The treatment of the non-traumatic hemothorax is first to care for any shock that may be present. As the bleeding undoubtedly is diffuse and not focal in origin, there is probably never an indication for thoracotomy and vessel ligation. Aspiration is usually indicated after about forty-eight hours as blood left in the pleural cavity may form fibrin clots, the latter requiring thoracotomy. The entire collection should be removed in one or two aspirations as the fewer the punctures the less danger there is of infection.—*James J. McCort.*

BANNEN, J. E. Post-operative pneumoperitoneum. *Brit. J. Radiol.*, April, 1944, 17, 119-121.

There is more or less postoperative pneumoperitoneum after every abdominal operation. One causative factor is probably the habit some surgeons have of pulling up the abdominal wall to the last stitch which increases the air content of the abdomen. The conditions could be prevented or minimized by exerting gentle pressure on the abdominal wall before inserting the last stitch and in this way expelling the residual air. The free air is generally absorbed in seven days and is therefore harmless, but it may cause a more or less serious degree of respiratory embarrassment and may be mistaken for more serious conditions such as subdiaphragmatic abscess and perforated gastric or duodenal ulcer. A correct differentiation from these conditions may prevent a serious operation. Roentgenograms should be taken within forty-eight hours after an operation with the patient in the Fowler position. In this position the free air in the abdomen rises to the subdiaphragmatic region and can be seen as an aerated space 1 or 2 inches thick between the diaphragm and the liver and stomach. Roentgenograms of a case are shown.

Marked degrees of pneumoperitoneum are more apt to occur in gynecological operations where the patient has been changed from the Trendelenburg to the Fowler position and where a large amount of tissue has been removed as in hysterectomy. Postoperative pneumoperitoneum is always bilateral and unless lung complications have occurred the lung fields are clear and there is no irregularity of the diaphragm. When the condition is caused by gas-forming organisms, as in peritonitis and after a perforation, the diagnosis must be based on the acute history and the presence of gas in the abdomen before operation. The postoperative abdominal discomfort frequently attributed to gas distention of the bowel may be due to pneumoperitoneum and in that case enemas will do no good.—*Audrey G. Morgan.*

MOLONY, CLEMENT J. Postoperative pulmonary collapse in childhood. *Am. J. Dis. Child.*, Sept., 1943, 66, 280-301.

Molony presents 21 cases of postoperative atelectasis in children. The cases were collected from the records of two large children's hospitals over a period of ten years. He was not able

to find in the literature an inclusive report of this condition from a children's hospital. The etiologic factors for collapse following surgical procedures are discussed and a plan of treatment based on these several factors is suggested. He emphasizes the importance of atelectasis in the production of bronchiectasis, and believes bronchoscopic drainage in cases of persistent collapse is the proper treatment.

The 21 cases are analyzed from the standpoint of incidence according to sex and age, type of operation performed, anesthetic used, symptoms presented, day of occurrence following operation, and day of clearing. In regard to the causes he discusses bronchial obstruction by a plug of mucus; the effect of hypoventilation brought about by the great decrease in vital capacity following operation; decrease in body tonus caused by the decrease in tone of the thoracic muscles and the diaphragm following operation; the role played by allergy; and the effect which may be produced by the use of the closed system of anesthesia.

He tabulates the precautions against and treatment for postoperative collapse based on the various etiologic factors. The article is profusely illustrated with roentgenograms of the changes in the lungs of many of the cases.—*R. S. Bromer.*

IMBER, IRVING. A tumor occurring in the superior pulmonary sulcus. *Am. J. M. Sc.*, May, 1944, 207, 654-660.

This case report and postmortem study was made because it illustrates a superior pulmonary sulcus tumor in which the extrapulmonary origin of the tumor can be established, thus favoring the original contention of Pancoast that a primary tumor may arise in the pulmonary sulcus and that it may produce a definite clinical syndrome. The clinical syndrome described by Pancoast included (1) pain in the shoulder region, often radiating down the arm and eventually to the fingers; (2) Horner's syndrome; (3) local destruction of the first two or three ribs, and (4) atrophy of the muscles of the hand.

The syndrome described by Pancoast was present in this case. The clinical course from the onset of pain to death was extremely rapid, totaling only three and one-half months. Physical findings and symptoms of a pulmonary lesion, which usually have been strikingly absent in the report of cases, were present in

this case, apparently due to the large size of the tumor. The rapid growth exhibited by this lesion on roentgen examination is also somewhat unusual. None of the roentgen examinations demonstrated evidence of osseous erosion.

It was thought that the tumor mass in the pulmonary sulcus at postmortem examination was undoubtedly extrapulmonary and was so proved by microscopic section. Dr. McFarland reviewed the histologic sections of this patient. He expressed the opinion that this tumor was composed of cells which are squamous epithelial cells, but did not reach the prickle stage and that the adrenal medullary tumors and the sulcus tumors were of the same cell type. From the history obtained it is not possible to state whether the Horner's syndrome preceded the onset of scapular pain or whether it followed the onset of pain.—*James J. McCort.*

OLCOTT, CHARLES T., and DOOLEY, SAMUEL W.
Agenesis of the lung in an infant. *Am. J. Dis. Child.*, May, 1943, 65, 776-780.

The authors report a case of complete absence of the right lung in an infant two months old. The diagnosis was made during life by physical, roentgenographic and bronchoscopic examination. The roentgenographic examination showed the cardiac silhouette and mediastinal contents in the right side of the chest continuous with the shadow of the liver. The left lung showed evidence of hyperventilation. No iodized poppyseed oil entered the left main bronchus.

Deficiency of a lung has been classified as of three types by Schneider. In type 1, there is no trace of a bronchus—true aplasia of the lung and bronchus. In type 2, the bronchus is represented by a blind pouch or a nodule of cartilage and fibrous tissue and there is no pulmonary tissue—aplasia of the lung. In type 3, the main bronchus is normal in size and shape and ends in a fleshy structure—extreme hypoplasia of the lung. The third type may be impossible to differentiate from secondary retraction of a previously expanded lung. In the case reported by Olcott and Dooley, at necropsy there was no recognizable right pleural cavity. The trachea formed an almost direct line with the left main bronchus. At the site of the normal branching of the right main bronchus was a barely recognizable pocket, not over 4 mm. in any dimension and no tissue of any sort was attached to it.

Agenesis of the lung is compatible with life. It is of diagnostic importance that the chest in patients with true aplasia of the lung is usually symmetric. Pneumonia of the remaining lung is often fatal. Cases have also been reported of the remaining bronchus being occluded by a foreign body.—*R. S. Bromer.*

CHILDRESS, WILLIAM G. Tuberculosis among hospital personnel. *Am. Rev. Tuberc.*, June, 1944, 49, 501-509.

Heimbeck reported positive skin reactions in only 52 per cent of incoming student nurses in Oslo, whereas at the time of graduation, 100 per cent of this group showed positive reactions to tuberculin.

Many other investigators have reported similar increments in sensitivity to the tubercle bacillus following contact. Workman's Compensation Acts have indicated the prevalent belief that contact with active tuberculosis provides a definite hazard—a hazard which pertains to those previously infected as well as to those not yet sensitized.

Periodic roentgen examination of the chest is considered a practical procedure, particularly for those who are required to work with tuberculous subjects; skin testing is not always practical.

This report pertains to observations conducted at the Grasslands, New York, since 1932. The bed capacity of the hospital was 800; 300 being tuberculous patients (housed in separate buildings interconnected by tunnels). The average employment numbered 750 (200 being permanently assigned to the section of tuberculosis). In all, 5,039 employees were studied, of whom 2,092 were subjected to contact with the disease.

Of the personnel without symptoms and with normal roentgen findings at the time of employment (45), 1.8 per cent of those exposed developed the disease and only 0.2 per cent of those not exposed did likewise.

Of the personnel showing active tuberculosis at the time of the first examination (14), 57 per cent had been exposed while 43 per cent had not been exposed.

Of those with a previous history of tuberculosis (65), 27 per cent of those exposed became re-activated while only 21 per cent of those not exposed did likewise.

Thus, the higher morbidities occurred among

the exposed versus the unexposed; considering all subgroupings, of 2,092 who were exposed, 3.5 per cent developed the disease, while among 2,947 without known exposure, only 0.54 per cent developed activity.

All types of personnel were concerned: physicians (13), nurses (45), attendants (10), porters (4), maids (3), kitchen workers (5), and laboratory workers (5).—*A. A. de Lorimier.*

DORMER, B. A., FRIEDLANDER, J., and WILES, F. J. Bronchography in pulmonary tuberculosis. I. Normal or questionable roentgenographic findings in lungs and positive sputum. *Am. Rev. Tuberc.*, Oct., 1944, 50, 283-286.

The authors have analyzed 5 cases wherein sputum examinations were positive though roentgen studies were considered negative or questionable.

Anteroposterior, lateral, and oblique film studies were accomplished; thereafter, bronchography was performed. With this latter procedure, the lesion was identified in every case.

The authors state that "the early lesion in tuberculosis is nearly always a bronchiectasis or a dilated bronchus terminating in a cavity." They conjecture that in pulmonary phthisis, the basic pathology is "bronchial block with subsequent pneumonitis and either abscess or bronchiectasis."—*A. A. de Lorimier.*

DORMER, B. A., FRIEDLANDER, J., and WILES, F. J. Bronchography in pulmonary tuberculosis. II. Radiographic black-out—evaluation of underlying lesions. *Am. Rev. Tuberc.*, Oct., 1944, 50, 287-292.

Previously, the authors have recommended bronchography for identifying the location of a tuberculous lesion when the sputum is positive though the roentgen studies be considered normal or indefinite.

This is a similar study but pertaining to cases having positive sputa and "black-out" areas, roentgenographically—opacities so great that the nature of the pathology cannot readily be discerned.

Bronchography was applied to 7 such cases where the character of the lesions could not be discerned by the conventional roentgenographic procedures. The contrast densities provided bronchographically served to visualize the character of the pathology. This procedure

is recommended, therefore, as a trustworthy substitute for tomography.

Again, the incidence of bronchial occlusion and of cavity formation in tuberculosis is emphasized.—*A. A. de Lorimier.*

SHAPIRO, ROBERT. Pulmonary tuberculosis in Navy recruits. *Am. Rev. Tuberc.*, June, 1944, 49, 485-489.

It is estimated that since the last great mobilization, the Federal Government has expended well over one billion dollars toward pensioning and compensation payments of service connected disabilities due to tuberculosis.

The attributes of photofluorography are expounded with respect to its value for screening. Its application is recommended to the extent of re-examination frequently. The author suggests that when developing an acquaintanceship with this procedure, the examiner should resort to standard procedures such as the use of the 14×17 inch film, frequently in the beginning; that such a policy should provide acquaintanceship with pitfalls and artefacts and that thereafter the need for 14×17 inch films will be reduced to approximately 0.5 per cent of the cases examined.

The factor of fatigue must be considered. Each examiner should identify his own fatigue threshold, and rest accordingly. With adequate precautions, the author estimates that with the use of the 35 mm. single film, misses should be kept to within 1 to 2 per cent.

The criteria for rejection by the Navy are cited; essentially, these including: any evidence of reinfection tuberculosis; evidence of activity of the primary phase or of an extensive primary lesion such as might later produce disturbances, or evidence of fibrinous or serofibrinous pleuritis.

This analysis is based upon a study of 50,100 photofluorographic examinations of candidates for Seabee duty with the Navy (many being of the fourth and fifth decades of life—and all having passed preliminary physical examinations).

The incidence of reinfection tuberculosis was believed to be 0.87 per cent; that of calcified primary tuberculosis, 10.7 per cent (5.3 per cent merely showing calcifications in the hilar lymph nodes; 5.4 per cent, both hilar adenopathy and calcifications in the parenchyma).—*A. A. de Lorimier.*

ABELES, HANS, and PINNER, MAX. Accidentally discovered pulmonary tuberculosis. *Am. Rev. Tuberc.*, June, 1944, 49, 490-500.

Chest surveys accomplished by roentgenography have revealed lesions in subjects in whom no illness had been suspected. Some of these lesions may be readily identified as tuberculosis; others may be so identified with the support of corroborative studies, while some remain uncertain as to the exact nature of the pathologic condition.

This report is based upon 91 cases of unsuspected lesions wherein the roentgen evidence was identified by corroborative hospital studies. Twenty-nine of the examinations were conducted among candidates for the Civil Service; 25 were merely contacts; 14 were candidates for employment to industry; 8 were included in a school survey; 6 were applicants for hospital employment, and the rest, similar healthy appearing adults seeking examinations in connection with insurance, premarital status, etc.

Only 67.4 per cent of the cases showing definite evidence of tuberculous activity had noticed any symptoms. The most common symptoms were of fatigability or occasional hemoptosis. Even after the diagnosis was established, in many of these cases, there was no substantial disturbance of wellbeing until as long as two years. Physical examination revealed definite findings in only 35 of the 91 cases (though 28 had minimal lesions; 40 moderately advanced, and 23, far advanced lesions). Roentgen studies indicated bilateral lesions in 47 of the cases; unilateral, in the right lung, in 31; unilateral, in the left lung, in 13. Sixteen of the cases showed definite cavities—all of which revealed tubercle bacilli when studied by direct smears or concentration tests.

The sputum was routinely examined first by direct smear; thereafter if negative, by concentration studies and possibly by culture or gastric washings. Using one or another of these methods (repeated studies being necessary in many of the cases), the tubercle bacillus was isolated in 84.6 per cent of the group.

Thirty-seven of the patients developed a white blood count in excess of 10,000; 54 showed a sedimentation rate in excess of 9 mm. for the first hour (Westergren method).

Determination of activity of a lesion was based upon: (1) roentgen evidence (serial studies, with consideration as to progression or

regression of the visualized lesion)—indicative in 90.7 per cent of the group; (2) sputum studies—with demonstration of the tubercle bacilli in 89.5 per cent; (3) blood counts and sedimentation rates—indicative in about 60 per cent.

Thus, the authors emphasize the particular value of roentgen studies and bacteriological examinations and the consideration of the clinical symptoms. Among the cases of inactivity, examinations of the sputum, guinea pig inoculations, white blood counts and sedimentation rates were negative.—*A. A. de Lorimier.*

MITCHELL, EARL B., and THORNTON, T. F., JR. Lower lobe bronchiectasis associated with tuberculosis. *Am. Rev. Tuberc.*, Jan. 1944, 49, 38-47.

The mortality from lobectomy is now reduced to 5 per cent or lower in several large institutions. Increasing numbers of patients with bronchiectasis are accepting this operation which offers greater relief in most instances than methods of medical management. One must bear in mind that a similar procedure in patients with tuberculous bronchiectasis carries with it a mortality of 18 per cent. Furthermore, such distressing complications as persistent draining sinus or fistula, tuberculous spread, and tuberculous empyema occur in about one-third of the patients. In spite of this risk, there is a definite indication for surgery if the tuberculosis seems stationary in the remainder of the lung fields and the symptoms of bronchiectasis are severe.

The fact that tuberculosis has so frequently been the underlying disease in bronchiectasis of the upper lobes and has not been found in lower lobe bronchiectasis has given rise to a widely accepted and reasonably accurate rule of thumb—that bronchiectasis limited to an upper lobe is tuberculous and limited to a lower lobe is non-tuberculous. The incidence of tuberculous bronchiectasis has not been determined accurately. The 5 cases reported by the authors represent approximately 5 per cent of all the patients with bronchiectasis seen at the University of Chicago Clinics in the past ten years.

Tuberculous lower lobe bronchiectasis should be suspected in any patient presenting one or several of the following features: (1) suggestive history; (2) roentgenological evidence of apical

tuberculosis; (3) bronchoscopic finding of bronchial stenosis; (4) unilateral or unilobar bronchiectasis. However, the diagnosis can be made with certainty only if a positive sputum is obtained. Repeated, careful sputum examinations in all patients having bronchiectasis are mandatory. If the diagnosis can be made early in the course of treatment, the authors believe that judicious use of thoracoplasty or lobectomy, or a combination of these procedures, will give favorable results in a high percentage of cases.—*John R. Hannan.*

BOBROWITZ, I. D. Round densities within cavities; lung lesions simulating the pathogenic roentgen sign of echinococcus cyst. *Am. Rev. Tuberc.*, Oct., 1944, 50, 305-312.

Two cases are reported wherein roentgenography of the chest revealed lesions showing a round uniformly dense focus surrounded by a concentric air space and membrane.

The author states that this feature has been described in connection with the echinococcus cyst, but otherwise not defined in the literature.

The lesions were visualized by conventional roentgenography—and even more clearly by tomography.

Both cases were subjected to surgery; in one, the process was identified as inspissated pus; in the other, as a blood clot.—*A. A. de Lorimier.*

ABDOMEN

CALTHROP, G. T. Cholecystography; pheniodol as a medium for the Graham-Cole test. *Brit. J. Radiol.*, Feb., 1944, 17, 60-61.

The chemistry of the various media used for cholecystography is discussed. Recently a new compound called pheniodol has been introduced. It is β -(4-hydroxy-3:5 diiodophenyl) α phenyl propionic acid. It was described by Dohrn and Diedrich in 1940 and placed on the market in Germany under the trade name of Biliselectan. Now a pheniodol of British manufacture is available. It is given only by mouth.

The author has tested its oral use in 100 cases. He finds it is a safe, convenient, economical and satisfactory means of examining the function of the gallbladder. The density of the shadow was generally as good as that after the intravenous injection of iodophthalein and the risks attending the use of that drug were eliminated.—*Audrey G. Morgan.*

BRYAN, LLOYD, and PEDERSEN, N. S. New gallbladder contrast medium; priodax. *Radiology*, March, 1944, 42, 224-225.

Tetraiodophenolphthalein has been the only contrast medium used in the examination of the gallbladder but it has a tendency to cause diarrhea, nausea and vomiting. A new medium called priodax has been produced. It is β -(4-hydroxy-3,5-diiodophenyl)- α -phenyl-propionic acid. It is excreted in a few days by the kidneys and does not collect in the colon as tetraiodophenolphthalein does. The minimal lethal dose is considerably higher than that of tetraiodophenolphthalein on parenteral administration and about the same on oral administration. It causes much less distress to the patient than the latter drug and is more effective as a diagnostic agent.

It has been given to 845 patients examined for disease of the gallbladder. Among these 227, or 27 per cent, were reported to have poorly functioning gallbladders. All of the gallbladders that showed impaired function roentgenographically with the new medium were found on operation to have some abnormality. One cancer of the gallbladder was found on operation.—*Audrey G. Morgan.*

PAUL, L. W., and POHLE, E. A. Oral cholecystography; a comparative study of the single- and divided-dose method with contrast media in liquid and solid form. *Radiology*, March, 1944, 42, 226-232.

The authors have been using sodium iodophthalein as a contrast medium in cholecystography, giving the first dose of 3.5 gm. after a regular lunch and the second dose of the same size after a fat-free supper. This gave a high degree of accuracy. There were few faint or questionable shadows.

They have now made a comparative study of this drug and the new contrast medium, priodax. They made 194 examinations on 148 patients, 114 of whom were given priodax and 80 iodophthalein. Priodax was given in a dose of 3 gm. Both media were used in 46 cases. It was found that the single dose method was as effective with both drugs as the intensified technique with a larger number of doses.

A table is given showing the results with the two drugs. The shadow-producing qualities of the two were about the same. There was slightly less nausea and vomiting after priodax but practically as much diarrhea (22.8 per cent

with priodax and 28.7 per cent with iodophthalein) though the diarrhea was somewhat more severe with the latter drug.

The simplified technique now used is to give one dose of the drug after a fat-free supper, eat no more after this and report for roentgen examination at 8 o'clock the next morning. If gas obscures the gallbladder pitressin is given; a cleansing enema may be given instead but is not as effective. Careful roentgen technique is of the greatest importance. The use of the rotating anode tube and the high-speed Potter-Bucky grid with short exposure times (one to two tenths of a second) was very helpful in giving clear, sharp shadows with sufficient contrast.

Priodax is easier to give than sodium iodophthalein as it comes in tablet form.—*Audrey G. Morgan.*

HEFKE, H. W. Cholecystography with priodax; report on 600 examinations. *Radiology*, March, 1944, 42, 233-236.

There are decided inconveniences in the use of tetraiodophenolphthalein as a contrast medium in cholecystography. It often causes diarrhea, nausea and vomiting. Vomiting may be so severe as to cause loss of contrast material and failure of visualization. A new drug called priodax has been introduced. It has a 52 per cent iodine content and the clinical dose of 3 gm. is far below the toxic level. The author has used this drug in 600 gallbladder examinations. He found that gas and the presence of the medium in the colon, causing confusing shadows, is not as frequent with priodax as with tetraiodophenolphthalein. Priodax was much better tolerated, and diarrhea, nausea and vomiting were less frequent and less severe with its use. Three out of 100 male patients complained of some burning on urination after priodax, due to the fact that it is excreted by the kidney. But urine examination in 30 patients showed no irritation of the kidneys. There was no evidence of any injury of the patients' health by the drug.

Priodax gave as good results as tetraiodophenolphthalein and in cases of non-functioning gallbladder even better. In 30 cases in which the first examination showed non-functioning gallbladder the dose was repeated. Only 1 of these patients showed a normally functioning gallbladder on re-examination while with tetraiodophenolphthalein 1 out of every 4 pa-

tients show normal function on twenty-four hour re-examination.

Surgery was carried out in 60 of these cases and operation confirmed cholecystography in all cases in which stones had been shown. Stones were also found in 1 case in which the diagnosis had not been made. In 1 case diagnosed as non-functioning gallbladder surgery showed normal function. The percentage of accuracy in the cases checked surgically was 96.7 per cent, which compares favorably with the findings after tetraiodophenolphthalein.—*Audrey G. Morgan.*

MUNK, JULIUS. X-ray appearances in amoebic hepatitis. *Brit. J. Radiol.*, Feb., 1944, 17, 48-53.

There are very few direct roentgen signs of amoebic hepatitis and therefore diagnosis must be made chiefly from indirect signs in the right half of the diaphragm and the lower field of the right lung. Diaphragmatic changes occur only in cases in which there is upward enlargement of the liver. This may be a generalized enlargement of the liver or only the subphrenic part may be involved.

Ten cases are described and illustrated with roentgenograms. From a study of the latter a division is made into three groups. In the first group in which only the lower anterior part of the liver is involved or in which the abscess is intrahepatic or subhepatic without general enlargement of the liver there are no roentgen signs. In the second group there were different degrees of total elevation of the right half of the diaphragm with different degrees of restricted movement, extending to complete cessation and with paradoxical movement on functional examination. There were also various degrees of atelectasis of the lower lobe of the right lung, pleurisy, enlargement of the intercostal spaces, blurring of the diaphragm and displacement of the heart. In the third group there were different degrees of bulging of the diaphragm, and generally restricted movement or no movement of the bulge on respiration, with increased movement in other parts of the diaphragm.

The importance of functional examination of the right diaphragm by Müller's and Hitzenger's tests is emphasized and the different appearances of atelectasis of the lower lobe of the right lung demonstrated. The value of the plate-like atelectatic foci demonstrated by Fleischner in 1936 as a roentgen sign is shown.

A roentgenogram similar to that of amebic hepatitis may be seen in other conditions such as the initial stage of pleurisy, all conditions of increased intra-abdominal pressure, a hydatid cyst or liver metastasis on the upper surface of the liver, paranephritic abscess or bronchostenosis, but there are usually differentiating clinical signs, which are discussed.—*Audrey G. Morgan.*

HILLER, GLENN I., and JOHNSON, RICHARD M.
Abdominal aortic aneurysm; rupture into the jejunum preceded by occult blood in the stool. *Am. J. M. Sc.*, May, 1944, 207, 600-606.

The patient, a white male, aged seventy-six, was admitted to the hospital on December 2, 1942. He had enjoyed good health most of his life and until five weeks prior to hospitalization, when epigastric pain and abdominal distention occurred with abrupt onset. At times the pain was cramping, knife-like and radiated across the upper abdomen. Nausea and anorexia were prominent features and on one occasion he had vomited a large quantity of bitter tasting greenish fluid material. Since the onset of symptoms he had lost 10 lb. in weight and complained of extreme weakness and dizzy spells. Physical examination did not reveal any masses or pulsations in the abdomen and admission blood count revealed 10.5 grams of hemoglobin per 100 cc.; and 4,600,000 red blood cells per cubic millimeter. Repeated stool examinations showed the guaiac test for occult blood in the stool to be positive. Roentgenologic examination of the upper gastrointestinal tract and the colon did not reveal any abnormalities.

In view of the fact that Golden has pointed out that blood in the stools without apparent cause is an indication for study of the small intestines, it might have been well if this patient had been studied by serial roentgenograms of the small bowel or by the method of the small bowel enema as advocated by Schatzki.

The patient died suddenly two weeks after admission. At autopsy an arteriosclerotic aneurysm of the abdominal aorta with rupture and perforation into the jejunum was found.—*James J. McCort.*

BRADLEY, J. EDMUND, and GREINER, D. JAMES.
Diaphragmatic hernia. *Am. J. Dis. Child.*, Aug., 1943, 66, 143-149.

A case of the rare type of congenital dia-

phragmatic hernia on the right side is reported. The only content of the hernial sac was a portion of the liver. The roentgenogram of the chest showed displacement of the heart to the left side with a dense shadow occupying the lower half of the right side of the chest that was later proved to be due to the upward displacement of the liver. The condition had existed since early fetal life. This was evident by the malformation or molding of the right lobe of the liver, which projected into the hernial sac, and the adherent maldeveloped, or fetal, right lung, which was closely associated with the sac. The case was typical of this type of lesion. The symptoms were almost entirely respiratory, appeared within two weeks after birth and varied in type and intensity until the patient's death, at the age of six months.—*R. S. Bromer.*

MORRISON, HOWARD J., and NEVILLE, R. L.
Omphalocele with congenital obstruction; report of case with Meckel's diverticulum. *Am. J. Dis. Child.*, May, 1943, 65, 781-784.

Omphalocele or exocelon is a true congenital umbilical hernia, containing intestine or abdominal organs. The authors report a case of omphalocele with congenital obstruction of the intestine. The intestines could not be reduced until the infant was anesthetized. The patient was operated upon when eighty minutes of age. Convalescence was uneventful, and at the age of fourteen weeks the infant weighed 12 pounds 11 ounces and appeared perfectly normal. An unusual physiologic phenomenon of the omphalocele's doubling in size when the infant began to cry was due to a valve-like obstruction, which caused air to distend the intestines within the omphalocele. Roentgen examination at the age of five months failed to reveal the presence of Meckel's diverticulum which had been found at operation. This was probably due to the fact that the diverticulum atrophied after the operation.—*R. S. Bromer.*

LEMONE, DAVID V., and COOPER, WILLIAM GRANT, JR. Total subphrenic abscess. *Radiology*, March, 1944, 42, 283-285.

Subphrenic abscess is generally an accumulation of pus in one or two of the numerous peritoneal pockets between the diaphragm and the mesocolon. A large number of the subdivisions of this space may be involved but in that case the patient usually dies. A case is here described in a farmer fifty-eight years of age

who fifteen years ago had had an attack of abdominal pain after eating, nausea and vomiting of bile. After recovery from this attack he was well for twelve years when he had recurring attacks of increasing frequency and severity. Five weeks before admission to the hospital he had an acute attack with prostration and violent nausea and abdominal cramps. On admission roentgen examination showed a translucent cavity involving the entire upper third of the abdomen from the diaphragm to the level of the fourth lumbar vertebra and from one lateral wall of the abdomen to the other. The entire liver, stomach and spleen were included in the cavity. The movement of the stomach was rapid and the barium mixture passed promptly through an opening in the duodenum into the cavity. After gastric lavage the abscess cavity was almost entirely cleared of the barium mixture indicating a free fistulous tract at the site of the perforation.

After closure of the fistula and drainage the patient recovered. Roentgenograms and a diagrammatic sketch show the findings.—*Audrey G. Morgan.*

PASTERNAK, JOSEPH G. Calcareous pancreatitis. *Ann. Int. Med.*, Nov., 1943, 19, 757-767.

In a discussion of the etiology the theory is presented that in acute pancreatic necrosis the fat necrosis has been shown to be due to the splitting of neutral fat into fatty acids and glycerin by the action of lipase that has escaped into the tissues from the pancreatic juice. The glycerin has been absorbed and the fatty acids combined with calcium to form insoluble soaps.

The consequences of calculi and calcareous deposits are atrophy and progressive fibrosis with more or less destruction of the parenchyma of the gland. As a result of obstruction of the ducts or destruction of the acinar tissue disturbances due to a deficiency of the pancreatic enzyme in the intestine may be conspicuous. Diabetes occurs when enough of the islands of Langerhans are destroyed. In 1 of the cases here presented a fragment of stone was found in the ampulla of Vater.

The clinical diagnosis of calcareous pancreatitis depends upon the roentgenographic demonstration of calcification in the pancreatic region. Pancreatic stones are usually sufficiently radiopaque to cast a shadow. When the clinical disease is not suspected shadows of stones in the

pancreatic region may go unheeded and without proper interpretation. In the present series 2 patients died of tuberculous bronchopneumonia and 1 of pulmonary abscess and gangrene. The fact that patients with prolonged pancreatic insufficiency are predisposed to pulmonary tuberculosis, suppuration and gangrene has been previously noted.

As regards treatment when the symptoms are principally those of pancreatic achylia, pancreatic enzyme therapy is highly effective. The response is characterized by a decrease in the frequency and bulk of the stools, associated with gain in weight and increased strength.—*James J. McCort.*

KAUFMANN, WILLIAM, and CHAMBERLAIN, DOROTHY B. Congenital atresia of pancreatic duct system as a cause of meconium ileus; critical review of the literature, with a report of one case. *Am. J. Dis. Child.*, July, 1943, 66, 55-67.

The authors report a case of meconium ileus in a three day old infant. Their patient, a white girl, born prematurely. Necropsy and further study of the pancreas, which was removed, established the absence of any intrapancreatic ducts, which made it probable that the excretory duct was also absent. The cause of the meconium ileus in their case seemed to be similar to that in the cases reported by Kornblith and Otani and others. Nevertheless, the fundamental lesion was somewhat different from that in cases hitherto reported, in that there was complete maldevelopment of all intrapancreatic ducts, ductules and acini while in all other cases of this type the ducts were present and often cystically dilated (cystic fibrosis).

The mechanism involved in the production of meconium ileus is thought to be as follows: Obstruction of the larger pancreatic duct, atresia of the pancreatic duct system or malformation of the entire exocrine system prevents the exocrine secretions of this gland from reaching the intestine. Acinar atrophy and fibrosis may result from the two first anomalies. Normal meconium, which is a dark brownish green, semisolid, viscid substance composed of mucus, bile, intestinal secretions, fat globules, cholesterol, vernix caseosa, epithelial cells and hair, requires pancreatic enzymes as well as bile for the maintenance of its normal composition and consistency. In

case the pancreatic enzymes are lacking in the intestine, a failure of digestion of fats and proteins in the meconium with resulting inspissation and hardening will occur. The tough, semisolid meconium accumulates in the intestine, since normal intestinal peristalsis cannot dislodge it, and fatal intestinal obstruction is the outcome.

Two greatly distended loops were found in the proximal part of the ileum. These loops were filled with thick, mucoid, sticky, dark green meconium which could be forced out of the lumen only by continued firm pressure. Its consistency was like putty. The enlarged portion of the ileum tapered off gradually until it averaged 1 cm. in diameter at the ileocecal valve. The latter was probed and was found to be patent.

The roentgen examination of the patient showed, after barium sulfate was introduced into the stomach through a tube, no definite dilatation of the stomach. The barium passed immediately into the duodenum. Two hours later the barium had appeared in the upper loops of the jejunum. Just distal to this, with the patient in the inverted position, a loop of small intestine was visible. There were multiple fluid levels in the gas-distended intestinal loops. A barium sulfate enema filled the rectum, the sigmoid flexure and the distal half of the descending portion of the colon. It was impossible to fill the remaining portion of the large bowel. A diagnosis of intestinal obstruction due to possible atresia of the lower part of the intestinal tract or due to compression from without was made.

The literature is reviewed in complete fashion and the possible causes of meconium ileus are discussed in detail.—*R. S. Bromer.*

MILLER, EDWIN M., GREENGARD, JOSEPH, RAYCRAFT, WILLIAM B., and McFADDEN, IRMA. Congenital atresia of the duodenum and of ileum; report of two cases with successful results following operation. *Am. J. Dis. Child.*, Sept., 1943, 66, 272-279.

The authors report 2 cases of congenital atresia of the ileum in which they performed successful operations. They also discuss congenital obstructions of the duodenum and the ileum (small bowel), contrasting the clinical pictures of the two conditions and emphasizing the essential points in the treatment of both.

They state that progress in the surgical

correction of congenital obstruction of the duodenum and ileum can be made only by close observation of the newborn infant during the first few days of life. Vomiting should not be considered as necessarily due to improper feeding. If it is persistent and remains constantly biliary, it is quite likely due to congenital obstruction of the duodenum. If vomiting persists and the material becomes brown and is associated with a progressive distention of the abdomen, there is in all probability a congenital obstruction of the lower portion of the ileum. In either case a roentgenogram of the abdomen may at once settle the diagnosis, and if it is followed by immediate accurate surgical measures there is a very fair chance of an excellent result.—*R. S. Bromer.*

PORTER, D. C. Megacolon. *Brit. J. Radiol.*, April, 1944, 17, 132.

True megacolon is comparatively rare. Two cases are described and illustrated with roentgenograms. The first was in a girl of seventeen with multiple congenital anomalies including slight shortening of the leg and an imperforate anus which was opened thirty-six hours after birth. The sigmoid condition was probably also congenital. She was extremely constipated until a lumbar sympathetic ganglionectomy was performed, since which time bowel action has been normal but the anatomical structure of the bowel did not return to normal.

The second patient was a woman of fifty-nine who has been constipated for as long as she can remember. The bowels act at intervals of four to five days and for several years the stools have been the thickness of a pencil. She has no pain on defecation and there are no signs of toxemia. A roentgenogram is given showing the difficulty of evacuating the dilated bowel in spite of daily colonic lavage.—*Audrey G. Morgan.*

GENITOURINARY SYSTEM

KIRSH, DAVID, and DIAZ-RIVERA, R. S. Perinephric abscess—a previously unreported complication of amebiasis. *Am. J. M. Sc.*, Sept., 1943, 206, 372-378.

After a thorough search of the American, English, and Spanish literature, the authors were unable to find a single instance of perinephric abscess complicating amebic dysentery. The urinary complications of amebiasis are said

to be cystitis, pyelitis, nephritis, urethritis, and kidney abscess.

The case reported here is that of a forty-seven year old Italian male who was admitted complaining of pain in the right side of the back and of the upper abdomen. For the past nine years he had suffered from relapses and exacerbations of a bloody diarrhea, accompanied on occasions by severe cramping abdominal pains which, in many instances, simulated appendicitis. Four months before admission the diarrhea recurred to a moderate degree with four to seven bowel movements a day, which on occasions consisted of only a small amount of mucus. On physical examination the liver apparently extended 17 to 18 cm. below the fifth rib. It, and the right costovertebral angle, were exceedingly tender. The stool examination was negative for *Endamoeba histolytica*. Roentgenographic studies revealed a slight elevation of the right diaphragm with haziness at the base of the right lung. The liver was reported not enlarged.

Eight days after admission laparotomy showed that the liver was diffusely enlarged but no pus or interhepatic or subdiaphragmatic masses were encountered. By blunt dissection carried around retroperitoneally to the perinephric space a large collection of pus was opened and drained. The cavity occupied the entire perinephric space. The pus was thick and yellow and was drained through a lateral stab wound. Ten days after operation blocked paraffin sections of the pus revealed *E. histolytica* in the vegetative form and this finding was confirmed three days later. The patient responded rapidly to a course of emetine hydrochloride. The authors feel it is possible that the parasite travelled through the lymphatics and localized in the perinephric space.—*James J. McCort*.

SHRADER, J. C., YOUNG, JOHN M., and PAGE, IRVINE H. Pyelograms in patients with essential and malignant hypertension. *Am. J. M. Sc.*, April, 1943, 205, 505-514.

This study was made to find the answer to two questions: (1) Is there a pyelogram characteristic of hypertensives? (2) Is the incidence of abnormal urograms in an unselected group of hypertensives greater than in an unselected group of normotensive controls? This study did not include hypertensive patients who showed evidence of surgical renal disease such as stone, tumor or infection.

The following definitions are given: the "intrarenal" pelvis is one in which the renal tissue wholly surrounds it and the ureteropelvic juncture is seen in the roentgenogram as part of the medial border of the shadow of the kidney. The ureteropelvic junction in a kidney with a "hilar" pelvis is separated from the medial border with the pelvis partly within it. The "extrarenal" pelvis appears to be outside the kidney, making the interrenal portion seem to consist entirely of calyx. Since the kidneys occupy a position of varying obliquity in the abdomen and the roentgenograms were taken in the conventional anteroposterior exposure, it is difficult to see how this classification can have any scientific value since the factor of projection is entirely ignored.

Each pyelogram was inspected for the following characteristics:

1. Location of renal pelvis as to whether it was intrarenal, extrarenal, or hilar.
2. Level of renal pelvis in relation to vertebral landmarks.
3. Renal torsion; complete or incomplete rotation.
4. Presence or absence of a right-angled ureteropelvic junction.
5. Capacity of the pelvis as judged from the comparative size of the shadow.
6. Size of calyces in relation to pelvic size.
7. Number of minor calyces.
8. Configuration of calyces and infundibula.
9. General shape of pelvis; triangular, square or rounded.
10. Axis of renal pelvis; normal oblique, horizontal or vertical.
11. Tendency toward intrarenal duplication of pelvis (bifid pelvis).

The upper limits of normal arterial pressure was arbitrarily taken as 149 mm. systolic and 89 mm. of mercury diastolic. The retrograde pyelograms of 100 hypertensives and 100 normotensives were studied. The retrograde pyelograms were made by the gravity method.

It was concluded from this study that the retrograde pyelogram of patients with essential hypertension does not differ significantly from those of normotensives. The incidence of urographic abnormalities in an unselected group of hypertensives appears to be no greater than in normotensives.—*James J. McCort*.

BARDEN, STUART P. Two unusual cases of urinary tract calculi. *Radiology*, March, 1944, 42, 285-288.

Two cases are described in which a roentgenogram of the abdomen showed multiple smooth, round shadows arranged in groups but not in the usual position for urinary tract calculi. In the first case the patient, a man of twenty-three, had gastrointestinal symptoms but no urinary symptoms. Physical findings and urine examination were negative. Intravenous urography showed absence of kidney function on the left side and a retrograde study finally showed a huge hydronephrotic sac in this region that contained multiple calculi. The patient recovered after nephrectomy. The specimen showed nephrolithiasis, hydronephrosis and a congenital polar vessel that caused constriction of the pelvis at the ureteropelvic junction. This case shows how long a urinary tract lesion may exist without causing urinary symptoms and that urinary tract disease is often manifested by gastrointestinal symptoms.

In the second case a man of twenty-eight had intermittent pain in the left loin radiating down the groin and into the left scrotum and pain in the hip, relieved by rest. Three years before he had had hematuria for a short time. There was no palpable abdominal mass and no tenderness in the loin. A survey roentgenogram of the abdomen showed multiple round grouped opacities in the midline overlying the sacrum. Intravenous urography showed a left obstructive uropathy, the point of obstruction by multiple calculi being at the distal third of the left ureter. Ureteral catheterization and retrograde pyelography showed that the calculi were in the ureter. Ureterotomy was performed and 72 stones removed. Afterward dilatation of the ureter was performed and the patient is in satisfactory condition.—*Audrey G. Morgan.*

SKELETAL SYSTEM

LEINWAND, IRVING, and DURYEE, A. WILBUR.
Chronic hypertrophy of the skin and long bones: an osteo-dermopathic syndrome. *Ann. Int. Med.*, Dec., 1943, 19, 1018-1028.

The characteristics of this syndrome are: (1) It affects young adults, beginning before the twentieth year, and is most apparent between twenty and thirty. (2) It is limited to males. (3) It is not related to occupation and there is no familial history or history of syphilis. (4) The general health is not affected. (5) The skin becomes thick and furrowed, especially over the forehead, face, scalp, hands and feet.

No other parts of the body are affected. (6) There is a thickening of the periosteum which is bilateral and symmetrical. (7) The extremities show considerable hypertrophy due to thickening of the skin and periosteum. (8) The hands are enormous. (9) There is a normal mental state and no loss of libido. In the patient presented here the condition began, about nine years prior to admission, with pain in the left ankle. A roentgenogram of the lower half of the tibia and fibula showed marked periosteal irregularity of both the tibia and fibula. There was no significant change in this appearance during the period of observation. A biopsy of the tibia was taken and the sections of decalcified bone showed a porositic cortex with the marrow spaces enlarged. The periosteal surface suggested some slight previous activity, i. e., young periosteal cells but no osteoclasts, now quiescent. The histological diagnosis was chronic productive inflammation of paraperiosteal tissues, paraosteitis and osteoporosis.

The differential diagnosis included hypertrophic pulmonary osteoarthropathy, familial acromegalic skeletal disease, acromegaly, osteitis deformans, chronic venous stasis, and syphilis. The presence of an excessive amount of estrogen in the male is suggested as a possible etiological factor in the syndrome of this patient.—*James J. McCort.*

RILEY, CONRAD M., and SCHWACHMAN, HARRY.
Unusual osseous disease with neurologic changes; report of two cases. *Am. J. Dis. Child.*, Aug., 1943, 66, 150-154.

The authors state the purpose of this report is to call attention to 2 unusual yet similar cases in which bizarre osseous changes and hyperreflexia were the outstanding features. They have been unable to find similar cases either in the literature or by consultation with persons versed in pathology of bone. They hope the report of the cases will call to light others and add to the understanding of the condition.

Both children, the subjects of the report, had a peculiar gait which was characterized by a straight leg, a wide base and a calcaneus limp; neither child could run. Ankle clonus and hyperreflexia were present in both children. One child showed extreme anorexia with emaciation; the other showed anorexia only. Both children fatigued easily. Roentgenograms of the long bones were similar, showing sym-

metrical areas of increased density and dilatation of the bony shafts with scattered areas of diminished density involving all the long bones. The base of the skull in one case was greatly increased in density. A biopsy of bone in the other case showed concentration of organic matrix and minimal evidence of bone resorption. There was no evidence of an inflammatory process.

In view of so many findings in common in the 2 cases, the authors regard it reasonable to suppose that in both there is the same underlying disease process.—*R. S. Bromer.*

ROBERTS, F. Nature and functions of the intervertebral discs. *Brit. J. Radiol.*, Feb., 1944, 17, 54-59.

Schmorl's work, based on the examination of some thousands of normal and pathological spines, gave the first thorough study of the intervertebral discs. The author says there is no denying the anatomical facts that Schmorl brought out but there is room for differences of opinion in regard to the mechanical and physiological principles on which he bases his conclusions. He discusses these principles critically and states his own conclusions when they differ from those of Schmorl.

He says there is no foundation whatever for the belief that the nucleus pulposus has any power of expansion. Nor is it elastic in the true sense of the word, which means that a body has

the power to recover its original shape when a deforming force is withdrawn. The nucleus does protrude when it is bored into but this is due to tension of the capsule. It also bulges when the joint is opened horizontally, but this is due to tension of the fibers which make up its mesh. In these cases both internal and external forces are at work and it is not a true elasticity.

The presence of the nucleus makes it possible for pressure to be transmitted evenly from the lower surface of one vertebra to the upper surface of the next. The discs do not act as cushions when subjected to a vertical force unless they are flattened by that force, and this is highly improbable. But they do act as cushions in the sense that the fluidity of the nucleus permits of a passive change in the shape of the discs and therefore in the shape of the spine as a whole. This enables the muscles to take the strain of any sudden movement. In addition the discs act as distributors of tension. The tonus of the capsule keeps the nucleus under tension.

The evolution of the spine is discussed and, unlike Schmorl, the author believes there is no evidence that the assumption of the erect position has placed any additional strain on the spine.

Apparently these facts have little to do with radiology but the author believes the radiologist should study the function as well as the form of the structures he examines.—*Audrey G. Morgan.*



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LIPOMA OF THE CORPUS CALLOSUM* A CLINICOPATHOLOGIC STUDY

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THE corpus callosum appears to be one of the favorite sites of cerebral lipoma. The world's literature contains 30† cases involving the corpus callosum among a total of approximately 100 known examples of lipoma of the brain.

Most publications on cerebral lipoma have appeared in the European literature and the excellent paper by Krainer¹ (1935) is especially recommended. Practically all authors have limited their study to the pathologic and anatomic aspects of the problem and have advanced various theories as to the pathogenesis of cerebral lipoma.

The purposes of this contribution are (1) to survey the extensive literature on lipoma of the corpus callosum, (2) to describe its anatomic aspects and (3) to discuss certain roentgenologic features which may permit one to make the diagnosis of lipoma of the corpus callosum *intra vitam*.

A tabulation of all previously recorded cases is included (Table 1) and 2 additional cases are reported in full to illustrate the salient points of the problem.

CASE REPORTS

CASE 1. J.M. (No. 551516), male, aged forty-four, was admitted to the University Hospital on July 13, 1944, referred by Dr. J. Grekin, of Detroit. For the past two years the patient had suffered from frequent headaches and convulsive attacks. These seizures usually had been of left motor jacksonian type, but occasionally right-sided convulsions had also occurred. The attacks were frequently followed by headache, vomiting, and mental confusion. A few weeks prior to admission, a mild left hemiparesis had gradually developed.

On examination, the patient exhibited a mild organic brain syndrome with memory loss, intellectual and affective dulling, and tendency to perseveration. The ocular fundi were normal. Except for a left lower facial paresis on emotional innervation, cranial nerve function was not disturbed. There was a mild left spastic hemiparesis, being most noticeable in the left leg; also the right lower extremity showed slight increase of muscle tone. Diadochokinesis was slowed in the left hand. Deep reflexes were exaggerated throughout, particularly in the left upper and right lower extremity. The right abdominal reflexes were absent, the left ones diminished. Rossolimo's sign was present bilaterally, but Babinski's sign was

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† This includes the two observations presented in this paper.

TABLE I
REPORTED CASES OF LIPOMA OF CORPUS CALLOSUM

Number	Year	Author	Age	Sex	Anatomical Findings	Clinical Findings
1	1856	Rokitansky ²	26	F	Pea sized, on posterior part of corpus callosum	None
2	1856	Rokitansky ²	5	M	Cylindric lipoma	None
3	1858	Benjamin ³	32	F	Cylindric lipoma with calcification and ossification; corpus callosum atrophic	Hemiparesis, convulsions
4	1863	Virchow ⁴	20	F	Fat strip on raphe	
5	1863	Virchow ⁴			Along fornix	
6	1869	Parrot ⁵	2	F	Flat lipoma	None
7	1873	Chouppé ⁶	45	F	Multiple lipomas, one on each side of raphe, a third between olfactory bulb and midline	Headaches, vomiting, hemiparesis, convulsions, mental changes
8	1874	Coats ⁷	38	F	Flat lipoma	None
9	1887	Leichtenstern ⁸			Flat lipoma	None
10	1895	Pugliese ⁹	31	M	Flat lipoma	Mental changes
11	1897	Bostroem ¹⁰	39	F	Lipoma of genu	None
12	1902	Della Rovere ¹¹	43	F	Streak-like	None
13	1902	Würth ¹²	14	F	Large ovoid lipoma; corpus callosum and left cerebral hemisphere atrophic; calcification present	Mental deficiency, convulsions, hemiparesis
14	1902	de Steiger ¹³	37	F	Lipoma of entire corpus callosum; separate nodule in choroid plexus; calcification	Mental changes
15	1903	Kirkbride ¹⁴	54	M	Flat lipoma, connected with choroid, plexus; corpus callosum hypoplastic	None
16	1904	Bartel ¹⁵	15	F	Flat lipoma; 2 nodules in choroid plexus	
17	1905	Ernst ¹⁸	53	M	Flat lipoma with ossification; corpus callosum hypoplastic	None
18	1907	v. Sury ¹⁷	66	F	Cap-like lipoma with calcification; corpus callosum hypoplastic	
19	1910	Abrikossow ¹⁸	3	M	Lipoma of corpus callosum; two nodules in choroid plexus	
20	1920	Körner ¹⁹	44	F	(Quoted by Krainer) no data available	
21	1921	Huebschmann ²⁰	3	M	Lipoma of genu; posterior half of corpus callosum absent	Mental deficiency, convulsions
22	1928	Huddleson ²¹	46	M	Walnut-sized lipoma on genu with calcification; absence of corpus callosum and septum pellucidum	None
23	1932	Rubinstein ²²	30	F	Flat lipoma with calcification; separate nodules on choroid plexus; partial agenesis of corpus callosum and fornix	Mental deficiency, convulsions
24	1936	Juba ²³			Flat lipoma with partial agenesis of corpus callosum	
25	1938	Gander ²⁴	29	M	Fat strip on each side of raphe	None
26	1938	Fattovich ²⁵	75	F	Flat lipoma over entire length of corpus callosum	Senile psychosis, probably unrelated
27	1945	Ehni and Adson ²⁶	18	F	Ovoid lipoma at anterior part of corpus callosum; partial agenesis of corpus callosum	Convulsions; calcification visible on roentgenogram. Operated on as brain tumor. Autopsy

TABLE I—Continued

Number	Year	Author	Age	Sex	Anatomical Findings	Clinical Findings
28	1945	Ehni and Adson ²⁶	16	F	Posterior part of corpus callosum	
29	1945	List, Holt and Everett, Case 1	44	M	Ovoid lipoma in region of genu; posterior part of corpus callosum absent; calcification	Headaches, convulsions, hemiparesis. Lipoma surgically removed. Died 5 months later. No autopsy
30	1945	List, Holt and Everett, Case 11	3 days	F	Cap-like, covering entire length of hypoplastic corpus callosum; separate nodules in choroid plexus; calcification in adjacent brain tissue; septum pellucidum absent; malformed cortical convolutions; lumbosacral myelomeningocele; subependymal heterotopias of gray matter in lateral ventricles	Ruptured lumbosacral myelomeningocele with paralysis of lower extremities; hydrocephalus

negative. No sensory changes were elicited. The gait was mildly hemiparetic on the left.

Electroencephalography revealed a generalized epileptoid pattern with occasional bilateral discharges from the anterior temporal regions. This was interpreted as an indication of a deep lesion in the forebrain.

Roentgenograms of the skull showed persistence of the frontal (metopic) suture and

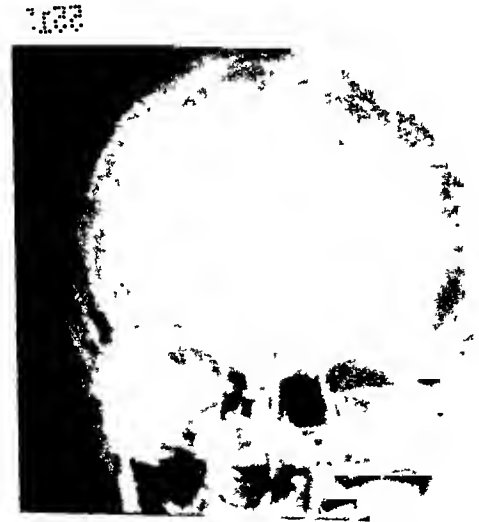


FIG. 1. Case 1. Roentgenogram of skull in frontal projection showing two crescentic lines of calcification outlining the lipoma. Note persistence of mid-frontal suture and undeveloped frontal sinuses.



FIG. 2. Case 1. Roentgenogram of skull in lateral projection. Area of increased radiolucency in mid-frontal region indicates lipoma (retouched).

absence of the frontal sinuses. Sagittal projections disclosed two crescentic calcium deposits surrounding the midline in the posterior frontal region (Fig. 1). The calcium deposits could not be identified in lateral views, but here an ovoid zone of decreased density occupied the mid-portion of the posterior frontal area (Fig. 2).

Ventriculograms suggested that the anterior portions of the lateral ventricles were spread by a midline mass, the periphery of which was partially outlined by the calcification described above. The posterior portions of the lateral ventricles were moderately dilated and the

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FIG. 3. Case 1. Ventriculogram in frontal projection showing the frontal horns of lateral ventricles separated by lipoma. The dilated third ventricle appears elevated due to agenesis of the corpus callosum (slightly retouched).

slightly enlarged third ventricle was displaced upwards (Fig. 3).

The diagnosis was made of a partially calcified tumor in the frontal midline area, associated with agenesis of the corpus callosum. A congenital lesion such as a lipoma, dermoid or complex teratoma was suspected. Exploration was decided upon because the patient's symptoms were progressive.

Operation was performed on August 25, 1944. Avertin-intratracheal ether anesthesia was used. A large right frontal osteoplastic flap was turned, crossing the midline to obtain adequate access to the region of the corpus callosum. After coagulation and sectioning of several veins connecting the frontal lobe with the superior sagittal sinus, and, after splitting of the falx, the midline structures could be clearly exposed. The posterior part of the corpus callosum was absent and instead, there was an opening leading into the lateral ventricles, covered only by arachnoid. The anterior part of the corpus callosum was replaced by an ovoid, encapsulated yellow tumor, the size of a large plum. It had the gross appearance of a lipoma. Demarcation from the frontal lobes was sharp. Both of the rather large anterior cerebral arteries and their branches were incorporated in the tumor capsule. The attempt to dissect the tumor *in toto* had to be abandoned because both anterior cerebral arteries deeply pene-

trated the growth. In an endeavor to save these vessels, the tumor was removed piecemeal, yet eventually it became necessary to clip the right anterior cerebral artery and also some branches of the left. After the inner core had been excavated, the firm capsule with its areas of calcification was removed from both frontal lobes. Following complete extirpation, it was realized that the tumor had replaced the knee of the corpus callosum and septum pellucidum, extending basally to the supraoptic area and posteriorly into the frontal horns of both lateral ventricles. After carefully establishing hemostasis, dura, pericranium, galea, and scalp were closed in layers with silk sutures.

Histopathologic examination proved the removed tissue to be a mature, encapsulated lipoma, containing many arteries and veins. Scattered calcium deposits resembling psammoma bodies were present in the adjacent brain and also in the connective tissue strands of the lipoma (Fig. 4).

The postoperative course was grave. For the first four days, the patient was comatose. His rectal temperature fluctuated between 102 and



FIG. 4. Case 1. Histopathologic picture of operative specimen showing mature lipoma with large blood vessels, pial capsule and areas of calcification in the adjacent brain tissue.

104°F., respirations between 36 and 44, and he hiccuped frequently. When consciousness began to return on the fifth postoperative day, complete right hemiplegia and paresis of the left leg were noted. It was assumed that, due to the surgical manipulation, thrombosis of both anterior cerebral arteries had occurred with resulting extensive softening, especially of the left cerebral hemisphere, and damage to the hypothalamus. In the course of several weeks, however, a gradual improvement took place and the temperature became normal.

On discharge six weeks after operation, the patient presented a profound organic brain syndrome with generalized psychomotor akinesis. Speech was monosyllabic and reiterative. A right-sided pyramidal-extrapyramidal hemiparesis was present, especially in the lower extremity, and also a slight paresis of the left leg. Bilateral forced grasping was noted. The patient was incontinent of urine. He could walk by himself, but with a bilateral spastic "marche à petit pas."

Three months later, he began to deteriorate gradually, both mentally and physically, and developed fever. He was then admitted to another hospital where he showed signs of progressive cerebral thrombosis or possibly late intracerebral infection. He died there, five months after the original operation. Unfortunately autopsy was not obtained.

CASE II. A female infant (No. 514642), aged thirty-six hours, was brought to the University Hospital on October 26, 1942, because of myelomeningocele. She had been delivered by cesarean section at another hospital. Examination revealed slight enlargement of the head (14 inches in circumference) with widely open fontanelles. There was a large lumbar myelomeningocele which had perforated spontaneously and drained spinal fluid. Both lower extremities were flaccid and completely paralyzed.

The infant was in poor condition throughout her stay in the hospital and she died on the third day. Permission for autopsy was obtained.

Autopsy. The pathological changes were found to be confined to the nervous system. There was a ruptured myelomeningocele (2.25 by 5 cm.) extending from the lumbar area to the sacrum, with acute purulent inflammation at its upper pole.



FIG. 5. Case II. Coronal sections of the brain showing the lipoma of the corpus callosum.

Examination of the brain showed the convolutions to be small and malformed. In coronal sections, the cortex was thinned and the lateral ventricles moderately dilated. The corpus callosum was replaced by a yellowish gray mass, measuring 2 by 2.25 cm. in the region of the genu and tapering posteriorly to 1.25 by 1.25 cm. in the splenic region (Fig. 5). The septum pellucidum was absent.

The fornix appeared to be incorporated in the tumor. Gray, pea-sized nodules were seen beneath the ependyma of the posterior horns of the lateral ventricles. All other parts of the brain and the rest of the body were essentially normal.

Microscopic Examination. There was acute purulent inflammation of the spinal cord and subcutaneous tissues at the site of the myelomeningocele. The cell layers of the cerebral cortex were poorly developed and the convolutions malformed. The subependymal nodules of the cerebral ventricles proved to be heterotopic islands of gray matter. The corpus callosum consisted of only a few thin strands

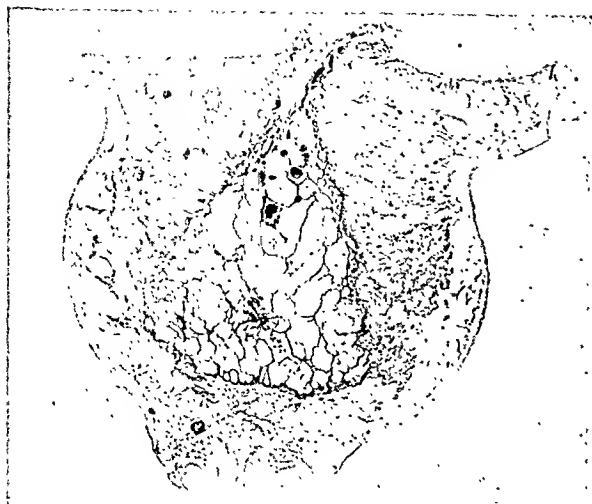


FIG. 6. Case II. Stained coronal section through callosal region at low magnification showing the relation of central lipoma to the underlying hypoplastic corpus callosum.

crossing in the region of the genu and splenium. The remainder was replaced by a vascular lipoma made up of fat cells of adult type (Fig. 6). Two rather large vessels, apparently the anterior cerebral arteries, passed directly through the center of the tumor. There were areas of calcification in adjacent brain tissue. The cerebellum was poorly developed. The fornix, basilar ganglia, and medulla were normal.

I. ANATOMIC CONSIDERATIONS

A. Macroscopic Anatomy. A lipoma of the corpus callosum is always situated on its dorsal surface and closely follows the contours of that structure. Most frequently, the tumor occupies the anterior part of the corpus callosum; less often it covers the entire length, or shows its greatest development in the splenial region. Since the lipoma is located beneath the leptomeninges, the arachnoid or pia of the sulcus corporis callosi forms what appears to be the capsule of the lipoma. Consequently, both anterior cerebral arteries are incorporated in the growth or its arachnoidal covering, sending many branches into the interior. The lipoma forms either an ovoid mass or a thin, streak-like layer; in some instances, it consists of two longitudinal columns with a central groove, corresponding to the median raphe. Anteriorly located lipomas

may extend to the lamina terminalis and involve the septum pellucidum and fornix.

There is considerable variation in size, the largest callosal lipomas observed attaining nearly the size of a hen's egg; the smallest, that of a pea. Occasionally, additional separate small lipomatous nodules were observed in the plexus choroideus (Rubinstein,²² Abrikossow,¹⁸ Bartel,¹⁵ de Steiger,¹³ our Case II) or in the region of the olfactory nerve (Chouppe).⁶

Most lipomas of the corpus callosum are perfectly demarcated from adjacent structures of the brain. In rare instances (Huddleson),²¹ they may give the appearance of infiltration into cerebral tissue. Calcification or even ossification occurs frequently (cases of Benjamin,³ v. Sury,¹⁷ de Steiger,¹³ Ernst,¹⁶ Rubinstein,²² Huddleson,²¹ Würth,¹² Ehni and Adson,²⁶ our cases). The calcium deposits may be macroscopically visible. They are found mainly in the peripheral portions of the tumor, its capsule or adjacent cerebral tissue. In Benjamin's³ exceptional case, the entire central core of the lipoma consisted of an osseous mass.

B. Histopathologic Structure. The microscopic picture of cerebral lipoma does not differ from typical mature lipoma or fibrolipoma found in other parts of the body. Histopathologic evidence of malignancy, such as infiltration, excessive mitoses, or atypical cells are absent. The occasional presence of young mesenchymal cells in the peripheral zone or capsule (Huddleson)²¹ does not necessarily mean active infiltrative proliferation, but may be a secondary reparative reaction of the damaged surrounding brain tissue.*

Cerebral lipomas never contain neural elements except those which originate from the neighboring brain and become accidentally included. It is also worthy of mention that dermal structures or cutaneous appendages never have been observed in cerebral lipomas. Calcium deposits may occur in the lipoma and adjacent brain as amorphous concretions,

* Analogous changes are found in the marginal zone of meningiomas.

as concentrically arranged bodies resembling psammoma bodies, or as islands of true bone. This calcification is generally interpreted as evidence of retrogressive change.

C. Associated Anomalies. Lipoma of the corpus callosum is often combined with other developmental anomalies of both the central nervous and skeletal systems. It is not surprising to find the lipoma associated with a defect of the corpus callosum. Total absence of this structure was observed by Würth,¹² Huddleson²¹ and by us (Case I); partial agenesis was noted by Benjamin,³ v. Sury,¹⁷ Juba,²³ Huebschmann,²⁰ Rubinstein,²² Ehni and Adson,²⁶ and by us (Case II). In Huddleson's case and our observations, the septum pellucidum was also absent, and in Rubinstein's case the fornix was hypoplastic. The question arises whether the defect of the corpus callosum is primary and leads to a compensatory formation of fatty tissue, or whether agenesis of the corpus callosum is secondary to the presence of the lipoma. Most evidence favors the latter view, *viz.*, that the lipoma develops at a very early embryonic period and interferes with the formation of the interhemispherical commissural system during the third and fourth fetal months. The callosal fibers then become deflected and instead of following their normal transverse direction, form a longitudinal fascicle (so-called "Balkenlängsbündel" of German authors). Since the corpus callosum develops in an anteroposterior direction, the presence of a lipoma inhibits formation of its posterior portion.

Other associated abnormalities of the brain have been found, such as atrophy of one hemisphere (Würth)¹² and malformation of the cortex (our Case II).

It seems to us of significance that the skeletal deformities occasionally associated with lipoma of the corpus callosum belong to the so-called dysraphic state. In our first case, there was persistence of the mid-frontal suture; in the second case, lumbosacral spina bifida and myelomeningocele were present. Huebschmann's²⁰ patient had a funnel chest. A most unusual observation

of Arnold²⁷ may be mentioned here, because it illustrates the combination of lipoma, dysraphic disorder and agenesis of corpus callosum in a nine-month-old boy: A large extracranial lipoma of the frontal region extended through the anterior fontanelle and gaping mid-frontal suture, and through a dural opening, into the cranial cavity. The tumor continued between both frontal lobes into the ventricular space. Corpus callosum, septum pellucidum and fornix were present.

D. Pathogenesis. Various theories concerning the morphogenesis of cerebral lipoma will now be reviewed in the light of available anatomic and embryologic evidence. It had been assumed that cerebral lipoma might develop by hypertrophy from pre-existing fatty tissue of the meninges (Virchow),⁴ or possibly by transformation or metaplasia of meningeal connective tissue (Pugliese),⁹ but these theories are now considered as untenable.

Recognizing its dysontogenetic character, Bostroem¹⁰ grouped cerebral lipoma with intracranial dermoid and epidermoid. He regarded all these lesions as heterotopic malformations of dermal origin and assumed that either the ectodermal elements of the original dermal anlage had disappeared, thus leaving a residual lipoma, or that only a few cells of the dermal anlage, with potentiality of differentiating into a lipoma, were displaced. Bostroem's hypothesis explains well the predilection of cerebral lipoma for midline structures, but it fails to account for the complete absence of dermal elements in these growths.

Verga²⁸ and Krainer¹, whose theory appears to be most acceptable to us, considered cerebral lipoma as a tumor-like malformation, derived from the primitive meninx. Krainer stated that, as a rule, the lipoma occurs in the leptomeningeal cisterns (e.g., the cisterna corporis callosi) and in the tela choroidea. He also emphasized the fact that the lipoma respects meningeal and neural structures and thus behaves like a malformation rather than a true neoplasm. If there is maldifferentiation or persistence of the primitive mesenchymal

reticulum surrounding the meningeal vessels, a lipoma may develop instead of the normal, fluid-containing leptomeninges. This concept agrees well with Wassermann's²⁹ fundamental work on the development of adipose tissue. According to this author, mature fatty tissue is derived from primitive perivascular reticulo-endothelium which, instead of subserving hematopoietic function, becomes specialized in the storage of fat. Since the perivascular reticulo-endothelium is ubiquitous and thus present in the primitive meninx, the formation of a pial lipoma can be easily explained. On the other hand, the rarity of cerebral lipoma and its selective location suggests the presence of additional local factors which are probably determined by developmental faults of the nervous system. Ehni and Adson²⁶ attributed the formation of lipomas (especially those of the spinal cord) to developmental disturbances of the neural crest. The frequent occurrence of cerebral lipoma in or close to the midline may be explained by a disturbed closure of the neuraxis in the posterior midline, associated with mal-differentiation of the primitive meninx. In other words, a dysraphic disorder is often an associated, if not predisposing factor for the formation of a lipoma.

II. CLINICAL CONSIDERATIONS

A. Incidence. Cerebral lipoma has no preference for sex or age. Its occurrence in early childhood is further evidence of its dysembryonic character. That lipoma has been incidentally encountered at autopsy in very old persons proves that it does not possess the active growth tendency of true neoplasms.

B. Clinical Symptomatology. Little is known about the clinical symptomatology of lipoma of the corpus callosum. The scarcity or even total absence of clinical symptoms and signs is not surprising, considering the small size of some of these lesions, their congenital origin, and lack of expansive growth. On the other hand, they may interfere with the circulation in both anterior cerebral arteries and thus cause clinical

symptoms. In some patients (Benjamin,³ Choupe,⁶ Würth,¹² Huebschmann,²⁰ Rubinstein,²² Ehni and Adson,²⁶ and our own), mental changes, convulsive attacks and hemiparetic signs were reported. In our Case I, motor jacksonian attacks with bilateral mild hemiparetic manifestations presented suggestive evidence of a parasagittal, possibly callosal, lesion with involvement of both frontal lobes. The syndrome was not clear cut, however, and did not correspond to the symptom complex of a vascular lesion of the anterior cerebral arteries. Signs of increased intracranial pressure reported by Choupe⁶ are, as a rule, absent, even though the lipoma is of sizable proportions.

It is certainly impossible to diagnose lipoma of the corpus callosum from clinical evidence alone, and its uncharacteristic symptomatology permits no clinical differentiation from cases of agenesis of the corpus callosum. It is therefore, fortunate that certain roentgenologic features of these lesions are so highly characteristic that in some instances, at least, a definite diagnosis during life is possible.

C. Roentgenologic Aspects. So far as we have been able to determine, the recent publication of Ehni and Adson²⁶ is the only one mentioning roentgenologic signs associated with lipoma of the corpus callosum. Sosman³⁰ presented the findings in 4 patients in whom he had made the diagnosis of such abnormality, but as yet his report has not appeared in print.*

Because the roentgen-ray coefficient of fat is appreciably less than that of any other body tissue, fat will be represented in the roentgenogram as a zone of increased radiolucency. In the case of a sizable intracranial lipoma, the tumor will reflect itself as a well demarcated area of decreased density standing out clearly against the denser background of the cranial vault. Ehni and Adson²⁶ did not mention this

* Sosman also described the roentgen signs of callosal lipoma in the discussion of a paper entitled "Midline Anomalies of the Brain" by A. P. Echternacht and J. A. Campbell. This paper was presented at the Joint Meeting of the American Roentgen Ray Society and the Radiological Society of North America in Chicago, Ill., Sept., 1944. (*Radiology*, Feb., 1946, 46, 119-131.)

feature although it appears to be present in reproductions of roentgenograms used to illustrate their article.

Calcification or ossification of a lipoma may partially or entirely obscure the characteristic radiolucency of the fat cells, but if this calcium deposit outlines the smoothly rounded periphery of the tumor, it furnishes another clue to the type of lesion present. In one of our patients (Case 1), the crescentic outer margins of the calcified tumor capsule were clearly discernible in sagittal projections of the skull, but no central zone of decreased density due to the presence of fat was evident (Fig. 1). In lateral projections of the same skull, however, the calcium deposits were too thin to be recognizable and the lesion was represented by a zone of increased radiolucency. Admittedly, this feature was seen only in retrospect (Fig. 2).

As previously stated, intracranial lipoma commonly arises in the anterior portion of the corpus callosum and is frequently associated with agenesis of the posterior portion of that structure, another condition in which diagnosis during life is possible only by employment of roentgenologic methods. Davidoff and Dyke³¹ were the first to describe the characteristic encephalographic findings in agenesis of the corpus callosum and they especially emphasized the concavity of the mesial margins of the widely separated lateral ventricles as an important diagnostic sign. This feature is even more pronounced when an associated space-occupying lipoma is present (Fig. 3). One should not assume that these two lesions are always co-existent. Only a minority of the verified cases of lipoma showed agenesis of the corpus callosum. Bunts and Chaffee³² reviewed 15 cases of agenesis of the corpus callosum discovered by roentgenographic means. The diagnosis was confirmed by craniotomy in at least 5 of these patients, but no reference was made to the presence of an associated lipoma in any of them.*

To recognize the roentgen signs of lipoma

of the corpus callosum, one must be constantly on guard to identify intracranial calcification and, more importantly, to prevent mistaking the pathognomonic zone of radiolucency for an area of bone erosion or even a fortuitous overlapping of prominent digital markings in the cranial vault. Since the density of air and of fat is almost identical, pneumoencephalography, so essential in the diagnosis of associated agenesis of the corpus callosum, is indicated only after plain skull roentgenograms have been obtained.

D. Neurosurgical Aspects. It is evident that lipoma of the corpus callosum is seldom, if ever, amenable to neurosurgical treatment, and only 2 cases of surgical removal are on record (Ehni and Adson,²⁶ and our Case 1). Although the excision of an ovoid or globular lipoma is technically possible, the crux of the situation lies in the fact that both anterior cerebral arteries are firmly embedded in the capsule or in the anterior of the tumor. Injury to these vessels is almost unavoidable when extirpation of the lesion is attempted. The resultant grave disturbances due to ligation or thrombosis of these vessels are well demonstrated by the postoperative course both in Ehni and Adson's patient and our Case 1. Ehni and Adson's patient died a few days after operation. In our own observation, the postoperative sequelae reduced the patient to a hopeless "brain cripple" and eventually led to his death five months later. The operation was undertaken because no accurate diagnosis was made as to type of tumor, and the important relationship of the anterior cerebral arteries to the tumor was not clearly realized preoperatively. We wish to state, therefore, that surgery is contraindicated if the diagnosis of lipoma of the corpus callosum can be made preoperatively.

SUMMARY

The literature on lipoma of the corpus callosum is surveyed and two case reports are added.

The anatomic features of these lesions

* One of our own observations of callosal agenesis was surgically verified but no lipoma was present.

are described and their pathogenesis discussed.

Even though the clinical symptomatology is not pathognomonic, the diagnosis of lipoma of the corpus callosum can occasionally be made during life by roentgenographic means. The roentgenographic signs consist of increased radiolucency of the tumor, calcification, demonstration of an expanding mass in the anterior part of the corpus callosum and agenesis of the posterior portion of this structure.

Surgical treatment of lipoma of the corpus callosum is contraindicated.

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NEWER INVESTIGATIONS OF RADIATION EFFECTS AND THEIR CLINICAL APPLICATIONS

PANCOAST LECTURE*

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INTRODUCTION

IT IS with a great deal of pleasure that I accept the honor of giving the Pancoast Lecture, because I doubt if any man had a higher regard for the personal or masterly qualities of mind and a greater capacity for friendship than Dr. Pancoast exhibited.

If it be true that we stand on the shoulders of those who have preceded us, certainly we who practice radiology should have a far vision, having stood upon the broad shoulders of Henry Pancoast. Not only was he large in stature but also in the breadth of his vision and the application of his active mind toward the solution of many of the problems which daily confront the radiologist. He exhibited a fine discrimination between merit and pretense, as shown by the type and quality of young men with whom he surrounded himself. He was a particular friend of the younger men in radiology and at any of the annual meetings one would see him in the center of such a group who were eagerly asking questions and receiving helpful answers. He was a man not given to flattery, and he accepted it with ill grace, and I am sure that if he were here this evening he would care much less for the plaudits bestowed upon him than for the subject of the discussion. He was interested in the larger aspects of radiology, as well as its minutiae, and it is with the latter that we are concerned in the topic for this evening, namely, "Newer Investigations of Radiation Effects and Their Clinical Applications."

When one speaks of "newer investigations of radiation" today, it is usually safe to assume that he means the amazing developments of modern nuclear physics

and artificial radioactivity. It is well to remember, however, that this is only one branch of atomic physics, and that another branch leading to advancement in radiation therapy has been progressing rapidly. In addition to fundamental physics, the advancements in technology today have put into our hands the means of understanding and making use of for the first time facts that may have been known in an inexact way for many years, as well as the means for gaining new facts. At the same time, there have been great advances in chemistry and physiology, without which the new fundamental knowledge of physics could not be integrated into an advance in medicine. Thus, as always, if science progresses at all, it progresses not in individual pieces, but as an integrated whole.

The age of advancement in the field of radiation therapy, which had its beginnings in the labors of Pfahler, Pancoast and other scientists, is therefore far from ended. Today, the radiologist is more than ever able to take all of the related researches from the fields of physics, chemistry and physiology, to correlate them, and to use them to build further knowledge on the foundation laid by these men.

When a patient is treated with a beam of radiant energy, nothing will happen unless some part of that energy is absorbed. It will be absorbed in part by both the normal structures of the body and by the disease process under treatment. The mechanism of the resulting reaction constituted an intriguing problem from the earliest days of radiation therapy, but curiously enough not until 1922 was there a worth while theory advanced for its

* The Pancoast Memorial Lecture, presented before the Philadelphia Roentgen Ray Society, November 5, 1942.

explanation. In that year, Dessauer published his "point heat hypothesis" according to which absorption of radiation is discontinuous, the energy ultimately becoming concentrated in a comparatively few discrete entities, within the cells. Only the energy liberated at these points was thought to cause any discernible effect through the relatively enormous amount of heat produced, whereas the energy absorbed elsewhere was considered to be of negligible biological significance. Since then, the point heat theory has been considerably expanded, and Crowther in 1938, on the occasion of the Twentieth Sylvanus Thompson Memorial Lecture, by correlating the newer findings, developed the so-called "target hypothesis." This theory, too, focuses attention on the discontinuous nature of roentgen-ray absorption and assumes that action takes place whenever one of the biological structures is "hit" by the radiation. But the "hit" is interpreted as the liberation of a pair of ions anywhere within the sensitive target area. Other investigators have given still different meaning to the word "hit," such as the absorption of a photon or, passage of an electron through some sensitive area.

In contradistinction to this discontinuous "point" or "hit" effect of the roentgen ray on biological objects, an action of a more generalized nature was assumed by adherents of a second theory which is most commonly known under the name of "poison theory." The general action was attributed to a photochemical effect of the radiation on the nucleus, leading to concentration of a certain poisonous material which through diffusion produces injury or death of the entire cell. Failla, in 1937, advanced the so-called "fluid flow theory," which also assumes a general effect through change in the ratio of the "radio ions" (rather than electrolytic ions) and the photochemical products on two sides of cytological membranes, thus creating a fluid flow which leads to change of cell properties.

In the following, certain experimental

data will be presented which aid in throwing additional light on the mechanism of the biological activity of the roentgen rays leading us a few steps farther toward the final solution of the problem which, I am confident, one day must come. Perhaps it may not be out of place to re-emphasize here a fact known to all of us, that the human cell constitutes one of the most intricate of all biological objects. It may be best construed as a system in which hereditary elements guide various types of physicochemical activities, depending on the influence of the environment. The hereditary elements are contained in the nuclear material and, according to Henshaw, are believed to represent specific entities located in linear arrangements along the chromosomes in a manner resembling beads on a string. Each entity, or gene, may change the course of life of the cell and, if the action of the roentgen rays injures them, multipolar cell divisions may be the result, with early death in the cell progeny.

The environmental factors may be located within the cell in the cytoplasm or without in the surrounding fluid. In both instances, through a diversity of physicochemical reactions, they may incite the hereditary mechanism, setting in motion particular phases of activity in which the cellular membrane must play an important rôle. Therefore, in studying the radiation effect on the cells, it seems worth while to pay special attention to certain physicochemical reactions which may influence the equilibrium between the intra- and extracellular medium, as well as to the function of the interlying membrane. Our experiments are in connection with such phases.

In one series, solutions of proteins, similar to those which were thought to constitute the most essential elements of our cells, were subjected to roentgen irradiation and studied for a breaking up of their molecules by measuring the osmotic pressure of the solution. The pressure so obtained is actually characteristic of two things, the number of particles of the solute

in the solution, and the character of the membrane. A truly semipermeable membrane must, of course, be completely permeable to the solvent, and completely impermeable to the solute. Such a membrane is also permeable to the ions of electrolytes, and it must be expected that in the case of a protein being broken down to low molecular weight amino-acids, or of amino-groups being broken off to form ammonium salts, these ions will penetrate any membrane which will hold the protein molecules and still be permeable to electrolytes. The direct measurement of osmotic pressure to any high degree of accuracy has always been attended with so much difficulty that most investigators have preferred to calculate this value from some more reasonably simple physical measurement such as the freezing point. For our purposes, none of these indirect methods would suffice, due to the fundamental nature of protein solutions, which undergo denaturation or other serious

changes rather easily with changes in physical state. Hence, a considerable amount of development work was necessary.

The final outcome was an osmometer, similar in outward form to the one de-



FIG. 1

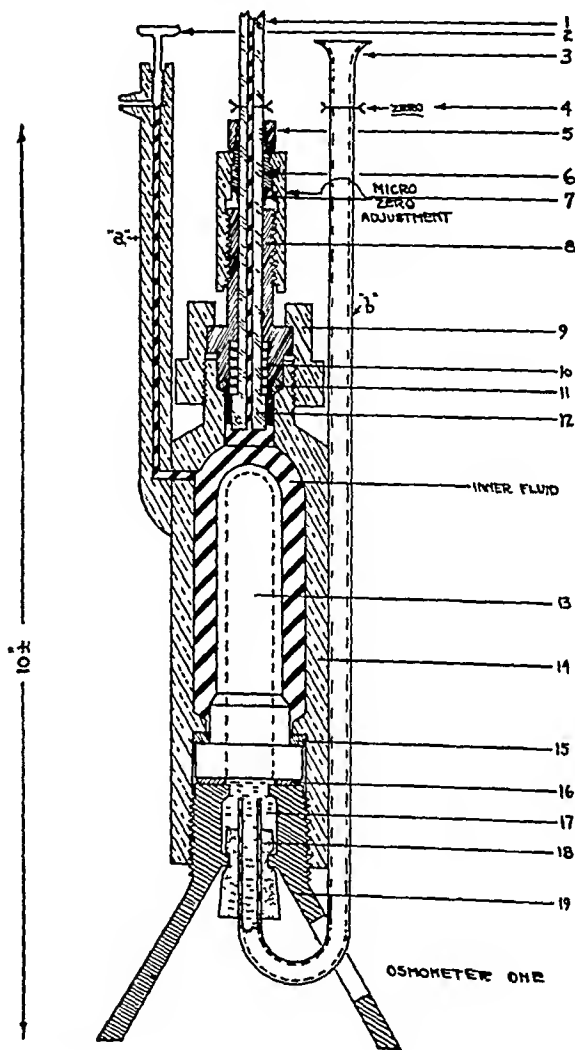


FIG. 2

veloped by Frazer and Myrick, but differing in a number of important respects. This instrument, which in actual use works inside of a constant temperature apparatus, is shown both assembled and dis-assembled in Figure 1. The porous cup, which carries the membrane, is made of sillimanite and fired to the hardness of a sparkplug. On the outer surface of this cup the membrane, which may be copper ferrocyanide, viscose or other material, is deposited by the appropriate method. The body of the ap-

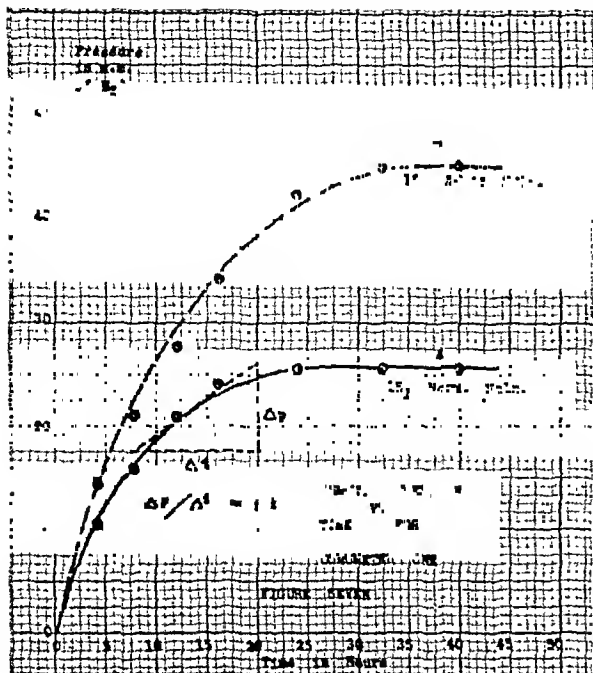


FIG. 3

paratus is a heavy brass shell, from the top of which a capillary manometer projects. The arrangement of the parts is shown in Figure 2, which is a cross sectional drawing. It can be seen that the volume of solution required is reasonably small, and particularly that the change in volume, and, therefore, the dilution error, is extremely small in proportion. A typical pair of curves for an experiment with this apparatus is shown in Figure 3. In this case, a 1 per cent solution of egg albumin in distilled water was irradiated with 12,000 roentgens at 550 kilovolts. This is, of course, a rather heavy dose of radiation but the change in osmotic pressure is 78 per cent, which is a rather startling amount. It is, however, in proportion to the dosage administered. A second osmotic pressure apparatus was used, this one built according to a design given us by Bourdillon, and using some special membrane material of a protein composition which he supplied to us. The advantage of this equipment is that it requires only a few drops of solution and works fast. It gives excellent results, and with the same membrane material will duplicate the results of the high pressure apparatus. The construction of the in-

strument is shown in Figures 4 and 5. This instrument was used with a different membrane, and the results shown in Figure 6 were obtained. At first glance, it might appear that some error has occurred, since the osmotic pressure of the irradiated solution is about 45 per cent lower than that of the unirradiated control. The explanation is quickly found, however, when the outer fluid is analyzed, for it contains the missing portion of the nitrogenous material. In other words, the osmotic pressure continued to rise, until the breakdown of the albumin reached a critical point. From this moment on, the membrane became permeable to the new chemical products, and the osmotic pres-

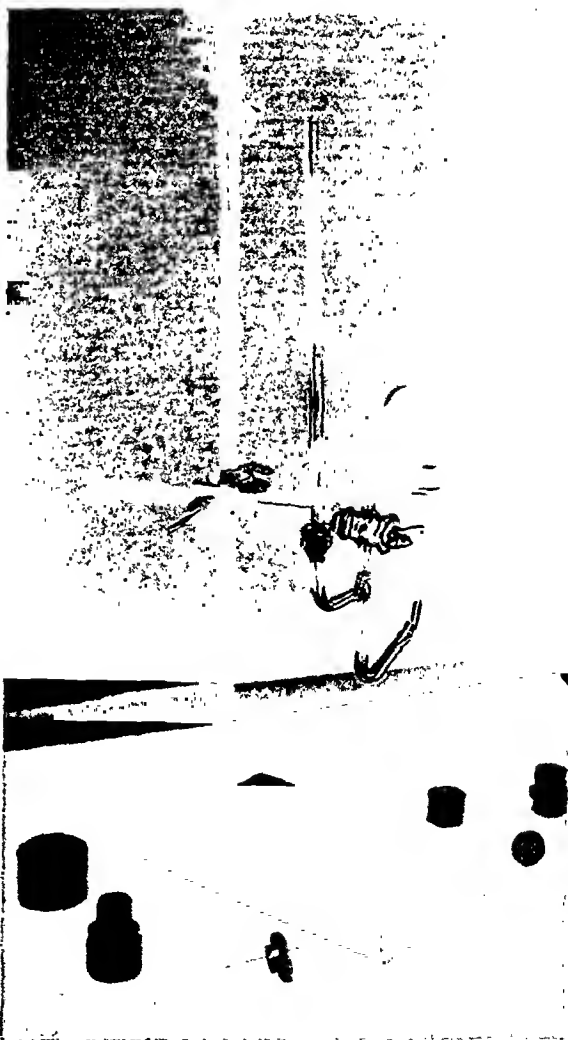
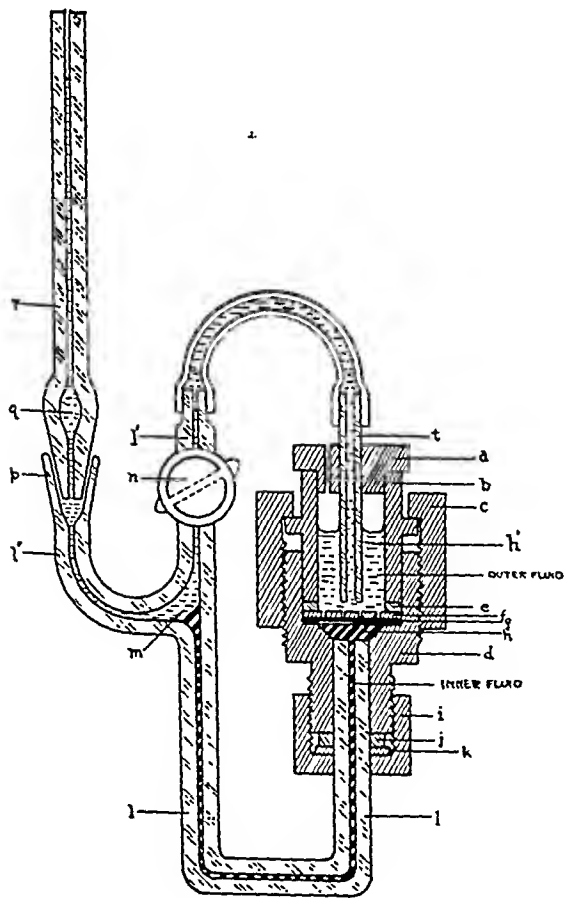


FIG. 4

sure started to decrease. A biological similarity is perhaps represented in the next two illustrations, which are stained sections from the brain of a dog. He lived for four days following the irradiation, and died in status epilepticus. The first (Fig. 7) is a specimen taken from an irradiated area in the motor cortex of this dog. The brain shows numbers of appreciably swollen cells. This intracellular edema demonstrates that the osmotic pressure within the cell has increased. The next illustration (Fig. 8) shows another section from the same dog, but at a point where the dosage was slightly larger, and here there are cells of exactly the same type and the same cortical layer, but this time, decidedly pyknotic. Originally, we thought that



OSMOMETERS TWO & THREE

FIG. 5. Reproduced by permission from Bourdillon.¹

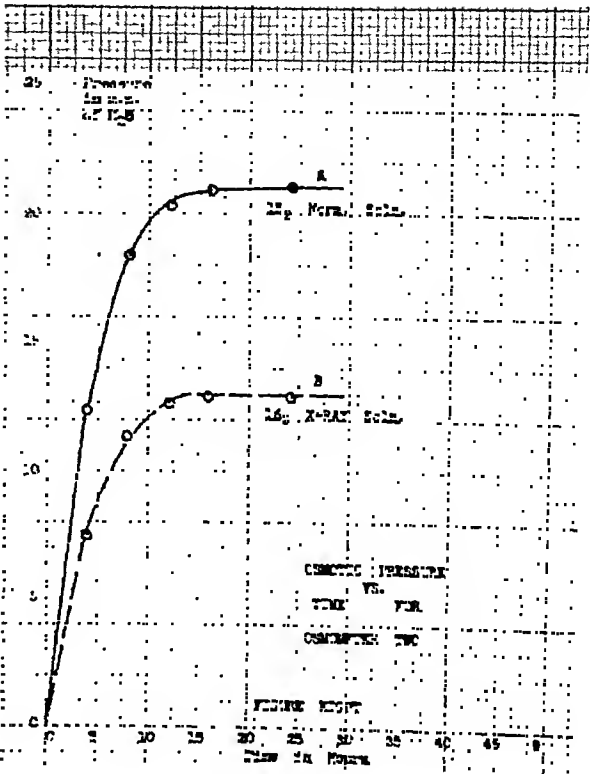


FIG. 6

these shrunken cells were the result of rupture of the cell membranes. But cells which have ruptured, probably due to excessive internal pressure, are easily found in these specimens and have quite a different appearance. The large pyknotic Betz cells shown here are not ruptured, for there is no chromatin matter outside the cell, and the walls themselves are continuous. We are led to believe, then, that a portion of the protein material within the cells was broken into such small fragments that the osmotic membrane of the cell wall could no longer hold them, as in the case of the laboratory experiment, or that the cell wall itself was affected.

Obviously, when we irradiate a biological system, we must bombard all of the parts simultaneously. Hence, the semi-permeable membranes which are the cell walls are affected at the same time as the protein material which they contain. Therefore, osmotic changes may result from injury to the cell wall rather than from injury to the contents.

This leads us to the second group of experiments, which are in connection with situations similar to those observed in cell membranes. Figure 9 shows a monomolecular layer of lipoid material prepared on the surface of water and exposed to only 600 r of 550 kv. radiation. In this case, the radiation enters through the bottom of the thin aluminum pan and passes through a 2 centimeter layer of water before hitting the monolayer. In this way, the beam is

It is also true that the exact physical state of the monolayer greatly affects its reaction and that, under some circumstances, reactions may be delayed so that their results appear only after the passage of time. Stenstrom and Vigness, in 1938, showed that when a drop of oil was placed on the surface of water and irradiated, it tended to spread out over the surface, and they showed further that this effect continued after irradiation was stopped, in

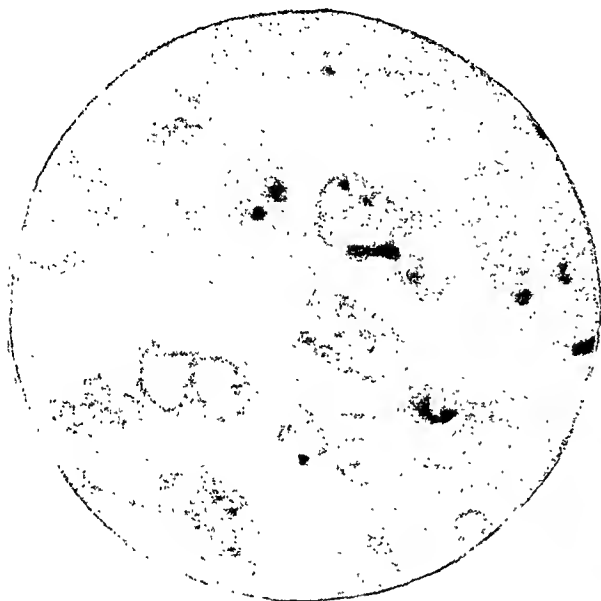


FIG. 7

brought to equilibrium with its secondary electrons. It can be seen at once that the beam, which entered through a small square portal under the pan, has imprinted itself clearly on the monolayer on top of the water.

Monomolecular layers which are exposed to water on one side and air on the other, and then irradiated in the laboratory, show different degrees of reactivity, depending upon their own chemical nature. The layer shown, which broke up under the influence of a very small dose of radiation, was prepared from the highly unsaturated lipoid material present in lanolin. A similar monolayer prepared from a completely saturated and highly unreactive substance, such as stearic acid, requires a much greater dosage before it shows any change.

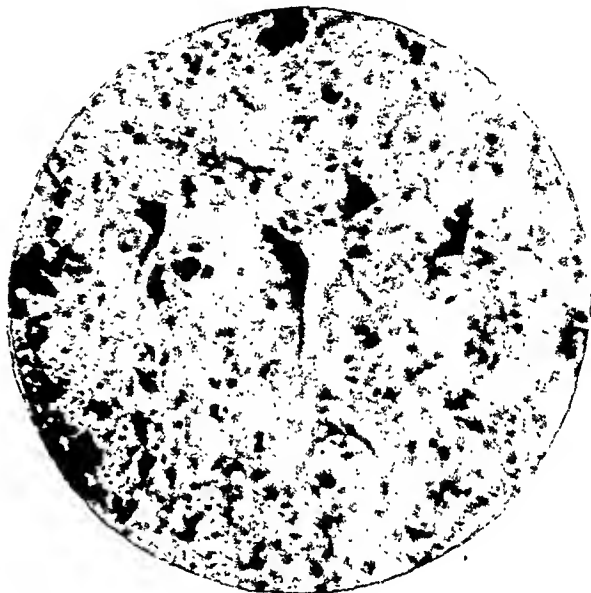


FIG. 8

some cases for at least twice as long as the time that the beam was on. Langmuir later showed that this was probably a direct oxidation effect. An example of such an effect is shown in Figure 10. In this case, the monolayer is like the preceding one, except that it is under somewhat greater pressure and was irradiated upon its upper surface. A dosage of 600 r of 550 kv. radiation was administered without any apparent effect. Twenty minutes later, the layer broke away, leaving an opening slightly smaller than the beam, but of precisely the same shape.

At the present time, the most important concept in quantitative biology is the idea of orientation of the protein and lipoid molecules; and this concept, for the first time, gives us a chance to understand the

substance and place it upon a perfectly clean surface of water the end, which is water-soluble, will enter into solution; we say it is "hydrophilic," but the "tail" of the molecule is definitely hydrophobic,

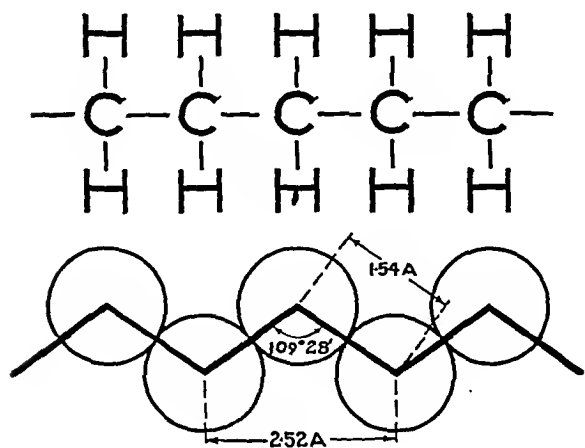


FIG. 12

and projects out from the surface. The result is a surface like the nap on velvet (Fig. 13). These molecules are called "polar molecules," due to the fact that

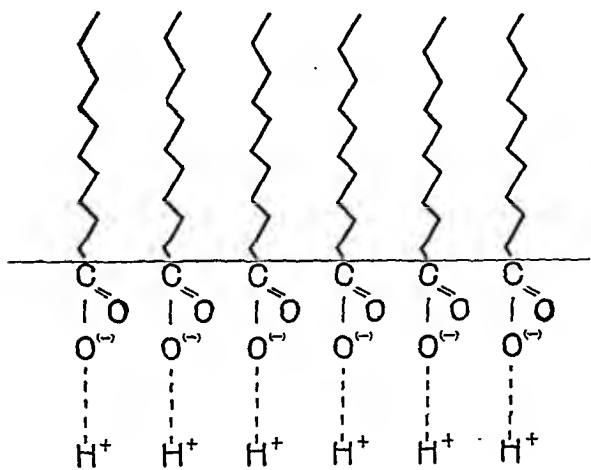


FIG. 13

they carry a group with a strong charge, electronegative in this case, on one end. They form themselves into monomolecular layers at any interface where the conditions are such that the polar end can ionize in one medium while the inert end is soluble in another; in this case, it is a water and

air interface, but an interface of water and oil would serve even better.

This alignment results in what is actually a two-dimensional crystal, and if this is true, we should expect the monolayer to have a refractive index, and a mechanical strength, for the inter-molecular and inter-ionic forces in crystals are relatively great, and show themselves grossly as resistance to cleavage and compression. Such is the case with these monomolecular layers. Figure 14 shows an apparatus used by Langmuir. Weights placed on the pan, *P*, of this apparatus balance the force exerted against the monolayer at the bottom. Monolayers of different substances, of

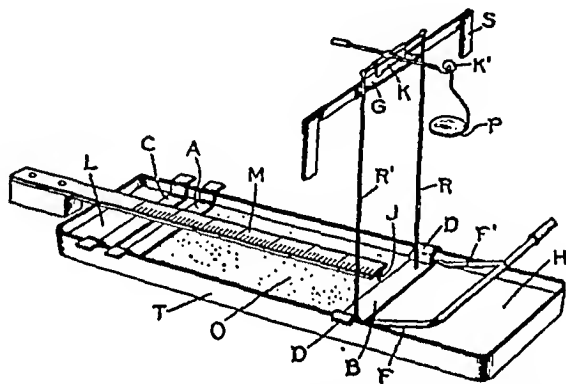


FIG. 14. Diagram of trough . . . showing surface pressure balance. Reproduced by permission from Langmuir.⁸

course, have different amounts of strength, just as one crystal may be harder to crush than another.

The facts taught us by the simple monolayer of a fatty acid help greatly when we come to consider the proteins. Here again, the chemist gave us the first basic information, but his methods could give us the precise composition of only the smaller molecular components, the amino-acid residues, which combine together to form great complex chains. These chains have molecular weights of the order of 35,000 and linkages of the greatest complexity. Chemical methods are always limited by the fact that they include hydrolysis and procedures which cause denaturation of proteins. They therefore give us the

structural building blocks without giving a picture of the building itself. Just as in the case of the simpler substances, however, roentgen-ray diffraction analysis furnishes an exact measure of the orderly spacings which occur in these molecules, and the fact that they form monolayers indicates that they consist in their natural state of molecular aggregates which can show both hydrophilic and hydrophobic groups. Figure 15 shows the form of some of the amino-acid groups of which these large protein molecules are built. The simplest one, of course, is alpha-amino-acetic acid (glycine). In the chart shown, the hydrophilic groups are to the right of the line drawn vertically through the molecular formulae. A number of very interesting things about these hydrophilic groups are immediately apparent. In the first place, every alpha-amino acid has both a negative and a positive group attached to the same carbon atom on the end of a hydrocarbon chain. Some of the more complicated ones also have either a positive or a negative one elsewhere in the chain. This gives rise to the familiar peptide linkage by means of which one of these acids can join with another. When we come to consider their

solubility in water and their chemical behavior, it is obvious that they will be attracted differentially by acid or basic solutions. Figure 16 gives a diagram of the protein chain. Between the two closely

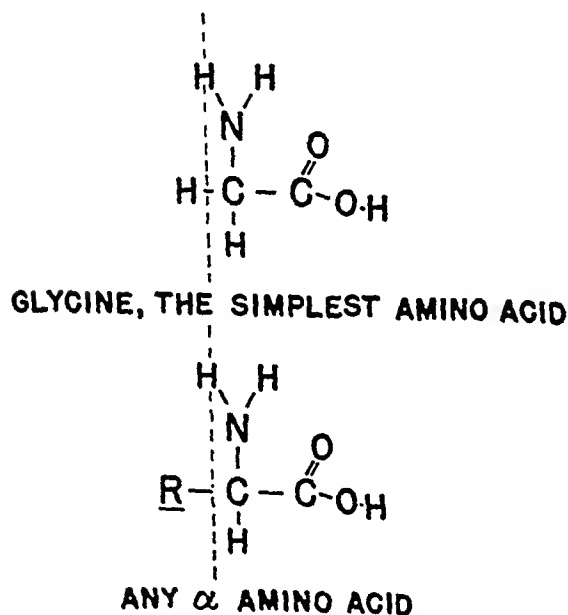
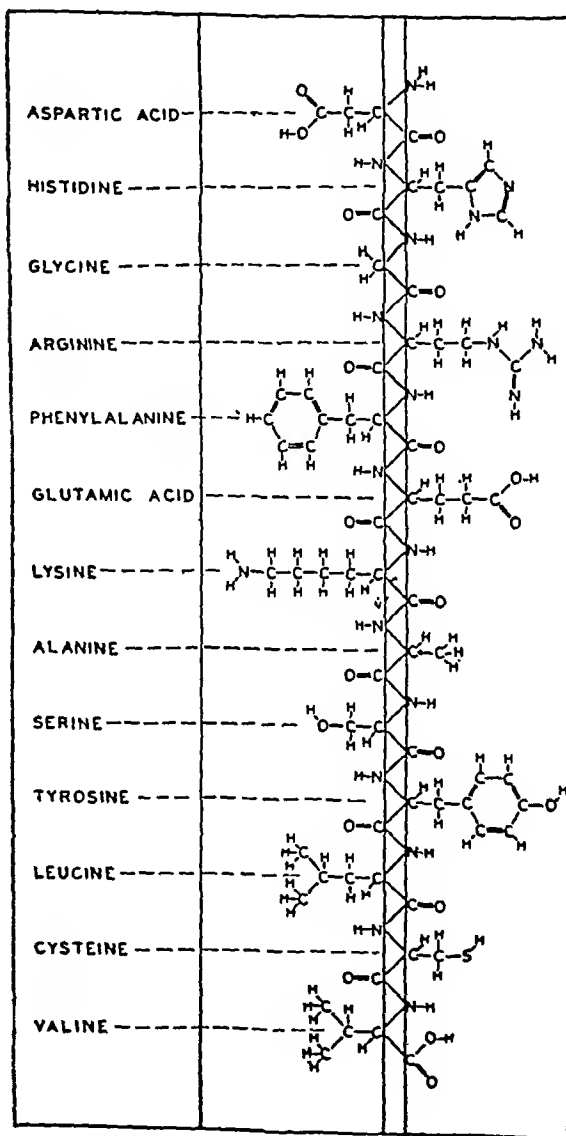


FIG. 15

FIG. 16. Diagram of a protein chain. Reproduced by permission from Sponsler.¹⁰

spaced lines on the right side of the figure is the carbon nitrogen chain which is called the backbone of the protein molecule. From each side of this chain there are side-chains extending each way in the figure. It must be remembered that, in actual fact, this is a three-dimensional structure and not flat, as we might expect from the

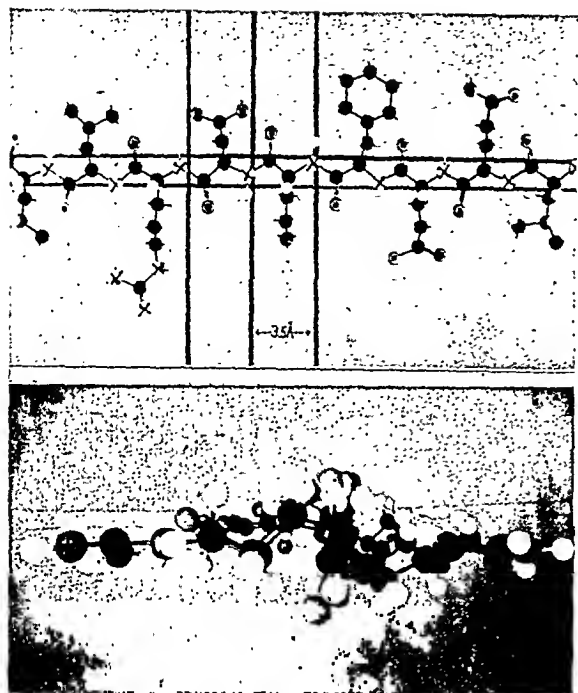


FIG. 17. (Top) A model of a polypeptide chain made to scale, showing eight amino acid residues. The back-bone and two residues are accentuated by the heavy lines. The black balls represent carbon atoms; those with a central dot, oxygen, and those with a central cross, nitrogen. The smaller white balls represent hydrogen atoms. (Bottom) An end view of a protein model. The vertical thickness in the middle is due to the back-bone and is about 4.5 Å. Reproduced by permission from Sponsler.¹⁰

appearance of this formula. A picture of a very accurately made scale model is shown in side view and in end view in Figure 17. When this molecule is oriented in a monolayer on the surface of water, the backbone

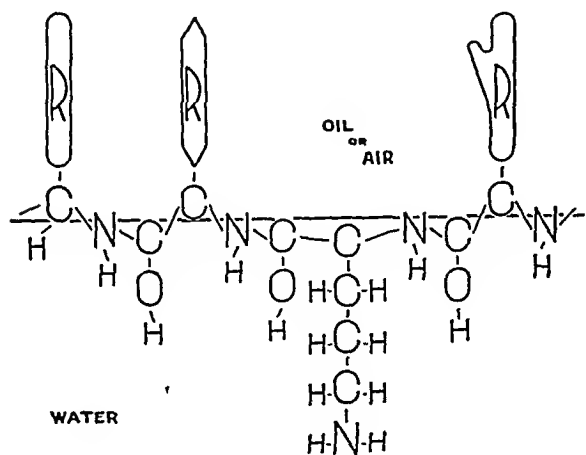


FIG. 18

lies parallel to the surface while the hydrophilic groups enter into solution, and the hydrophobic groups are repelled upward away from the surface and at angles dependent upon their valence linkage. Such an arrangement is shown in Figure 18, but now, also, there is a new situation due to the fact that there are two types of hydrophilic groups and also to the fact that, as in any straight chain compound, there can be rotation of side-chain groups around the backbone of the protein molecule. If the pH of the water is decreased

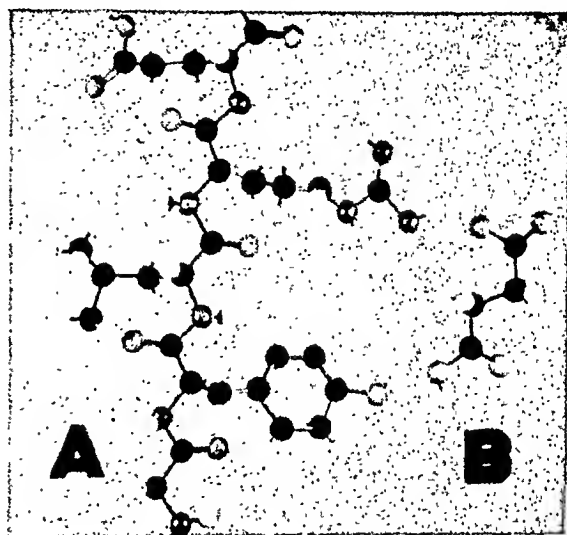


FIG. 19. Reproduction of models to show similarity of spacing, about 7 Å, which may exist between the active groups of succinic acid *B* and the terminal groups of the two residues arginine and tyrosine on the protein chain, *A*. Reproduced by permission from Sponsler.¹⁰

so that an excess of hydrogen ions is present, the amino groups will be strongly attracted while the carboxyl groups will be less attracted. In like manner, if we put some substance in water, which has a strong attraction for the negative groups, there will result a different spatial arrangement of the chain. This ability of the protein chain to rotate upon itself and orient possibly reacting groups together so they may combine is of the greatest importance, for in this manner not only are chemical combinations built up at the interface, but

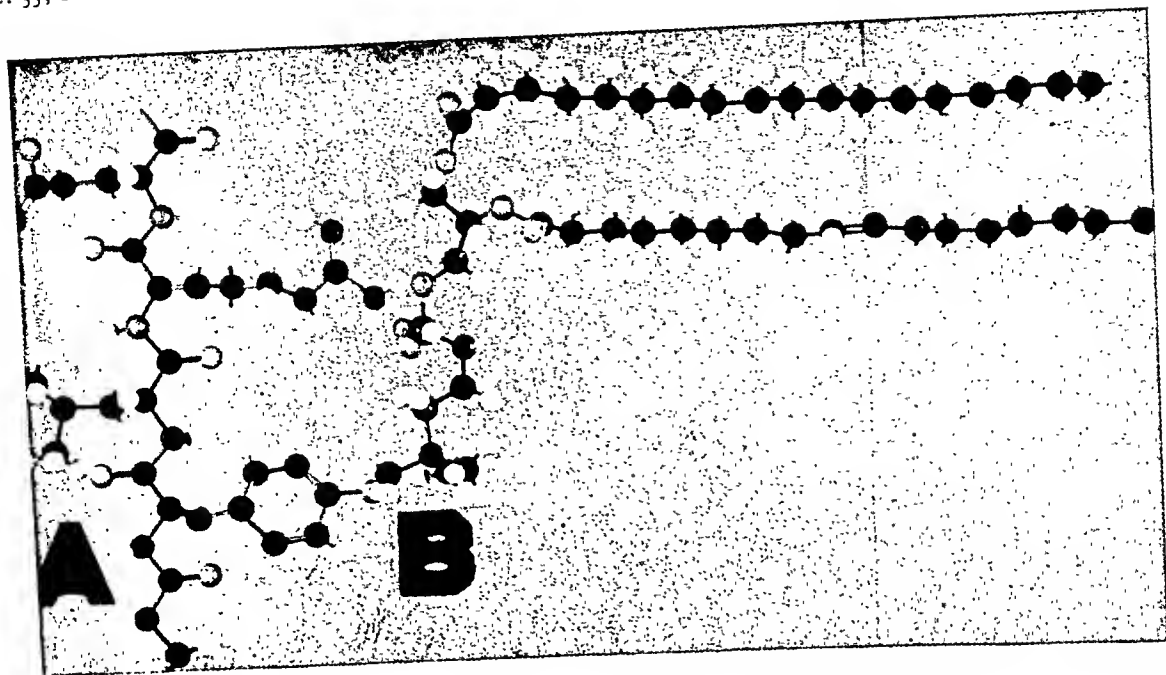


FIG. 20. Reproduction similar to that of Figure 19 except that the prosthetic group is a form of lecithin. Reproduced by permission from Sponser.¹⁰

chemical combinations between molecules, oriented into the same surface also occur, so that unlike the simple monomolecular layer of the aliphatic acid in which each paraffin chain projected upward like a single thread of silk in the nap of a cloth without relation to its fellows surrounding it other than to exert a repelling physical force upon them, the protein molecules combine themselves together into a continuous homogeneous sheet. The manner in which this may occur is illustrated in the following photographs of models, for which we are indebted to Professor Sponser. Figure 19 shows at *A* a part of a protein molecule consisting of two amino-acid residues, one of arginine and one of tyrosine. Reacting groups project to the right from the backbone and at *B* a simple molecule, in this case succinic acid, joins them together. This combining group need not be anything as simple as succinic acid. It can just as well be two reacting groups on the backbone of another protein chain, having the same spacing, and arranged in the same monolayer. Or, as in Figure 20, it can be a molecule of lecithin, which is a lipid. The fact which of all is by far the most important is that the "three musketeers" of the protein chain, the carboxyl carbon, the alpha carbon and the amino group, can shed the hydrogens of the amino and the doubly bonded oxygen of the carboxyl, and thereby gain four active valence bonds. Just how this comes about is shown in Figure 21. For convenience of illustration here we have greatly reduced the scale of the larger part of the molecule and exaggerated the size of the groups of three atoms involved in the reaction. It can be seen that when two of these groups combine they form the familiar hexagonal ring, as shown in Figure 22, and this ring still has combining power remaining. In this way the whole lacy fabric, known as the "cyclol structure," is built up to the form shown in Figure 23, which is taken from the work of Wrinch. The folding of this fabric to form a three-dimensional octahedron gives the structure of the globular proteins, so beautifully shown by Wrinch (Fig. 24) (insulin).

The fact that lipid substances will combine with protein monolayers, at last gives definite information as to the structure and the characteristics which determine

the function of the membranes of living cells. Obviously, we can form one monolayer on top of or beneath another which already exists. For example, a monolayer of aliphatic acid or lipid may have a protein monolayer formed below it in such manner that the amino groups of the protein attach to negative groups of the lipid, while the negative groups of the protein remain in the water. We then have an artificial cell membrane and the penetration into this membrane of either fat-soluble or water-soluble drugs and chemi-

the effect of the drug or chemical on an erythrocyte, a paramecium, or any cell which has a suitable membrane. Riedal has made the most careful and precise measurements of this sort, and by this means has been able to demonstrate the cell wall effects of many poisons, toxins, carcinogenic agents, and anesthetic materials. One single example of pertinent chemical knowledge which can be drawn from this type of investigation is perhaps not out of order. There is a well known correlation between fat solubility and

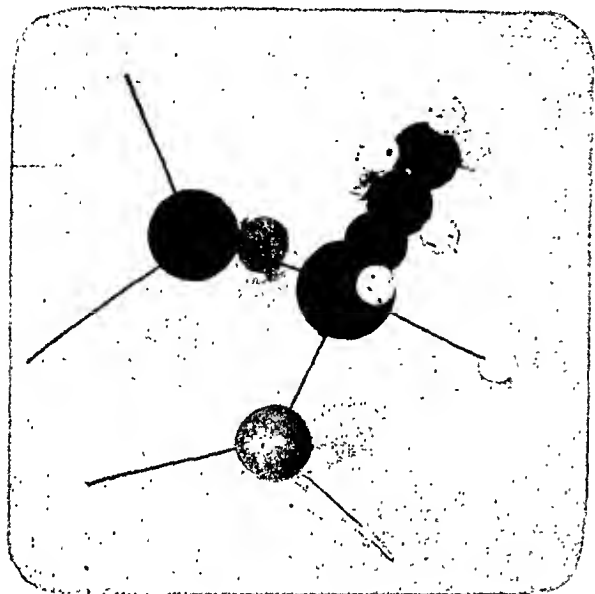


FIG. 21

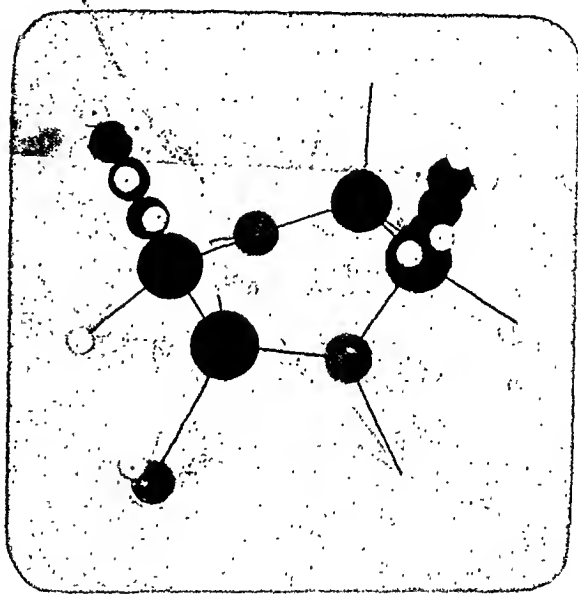


FIG. 22

cals can easily be tested. To get a precise comparison between this artificial cell membrane and a natural one, we have only to find a natural cell whose membrane has the same structure, and try the same reactions on the cell. In the artificial membrane, we can determine penetration by measuring the pressure of the monolayer exerted against a barrier, such as Langmuir's balance, or by measuring the refractive index, or by applying any of the precise physical methods by which we ordinarily detect reactions between molecules or penetration of a new molecule into a structure of another molecule. The physiological comparison is made by watching

anesthetic properties of certain chemical agents. Studies have also been made on arterial and venous oxygenation of the cerebral circulation of patients under the influence of these anesthetics, and it is known that the consumption of oxygen decreases far in excess of what is to be expected simply on the basis of the brain and body being at rest. If now we take a double lipid protein monolayer and treat it with this same anesthetic agent—in this case, cyclopropane—we find that the oxygen transmission of the interface is vastly reduced. In similar manner, various anesthetic agents have been studied, both on artificial monolayers and on individual

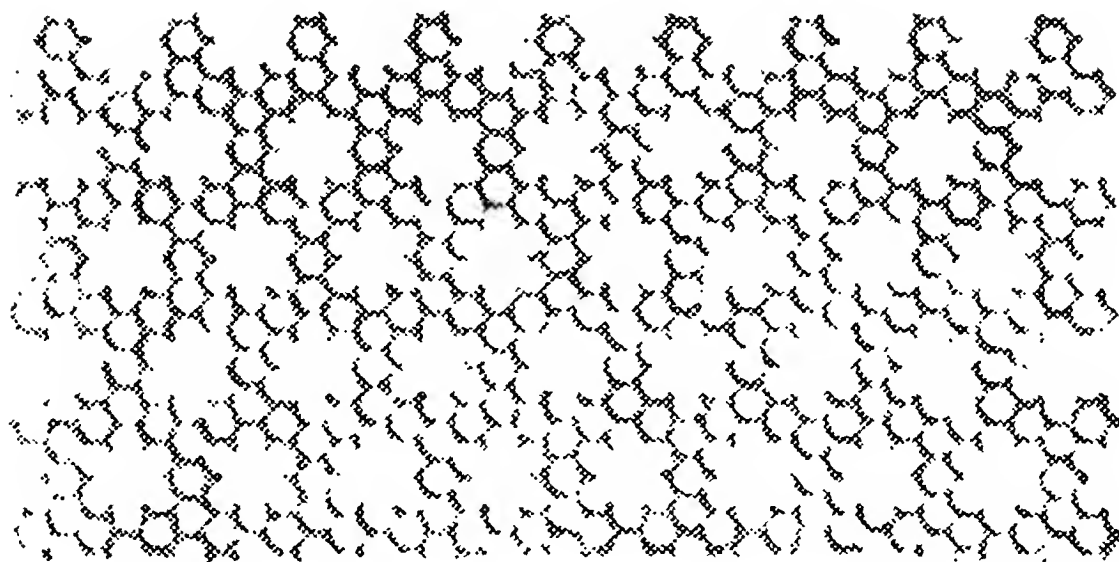


FIG. 23. The fragmentation of the cyclol fabric into oriented polypeptide chains. Reproduced by permission from Wrinch.¹²

cells. From the purely physical point of view, probably a more interesting fact is that in the monolayer there is an array of positive and negative molecular poles precisely lined up and oriented against each other. Obviously, an electrical potential must exist across the interface, and in the normal resting state this potential will be equalized by an arrangement of the free molecules on each side of the interface, so that this potential is brought to zero. This, however, is not a state of chemical neutralization but a dynamic state analogous to a battery without connections or a charged condenser. Through these studies, for the first time, it has become clear how the electrical potentials which seem to be the vital driving force, not only of the brain and nerve, but of all physiologically reactable components of the body structure, have their origin.

This brief outline of a few of the salient features of modern physical research on cell structure gives a general picture of the nature of cell membranes (and, as we shall show below, of a few intracellular structures). We see that they are not inert shells like the chitinous covering of the body of an insect, but are dynamic, living

entities having a complex structure both chemically and electrically. This structure is maintained in a somewhat precarious state of balance and can change in response to small physical and chemical changes of the environment. The disruption in this state of dynamic balance, which can be caused by ionization due to an energetic secondary electron plunging through these structures, may well be imagined.

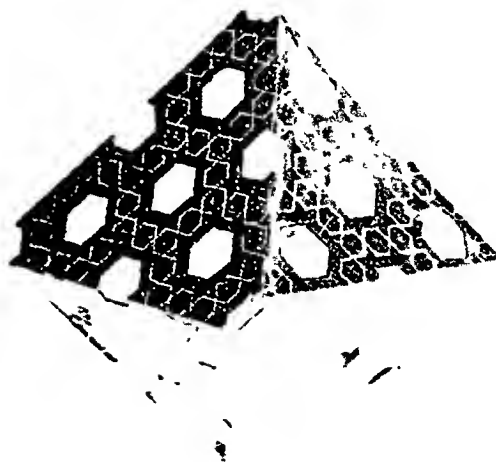


FIG. 24. The cyclol cage molecule, C_2 , comprising 288 residues in its skeleton. Reproduced by permission from Wrinch.¹²

A good experimental example in this respect is the lipoid, lecithin, one of the most important constituents of brain and nerve tissue. It is a highly polar molecule, which lends itself readily to the formation of monolayers or to the formation of highly oriented multilayers on glass. A layer of this substance built up in this way has very strong optical properties and its interference with a beam of polarized light is very clear and strong. If we build such a multilayer and expose it to radiation, we should expect any disruption in the molecular or intermolecular structure to show itself by disruption of the optical properties. The effect of roentgen irradiation on such an artificial multilayer is shown in Figure 25. Here, there is a layer of lecithin about 0.05 mm. thick which was exposed to a beam of radiation, 0.5 mm. in diameter, at just one point on its surface. The two upper fields in the figure show the same point in its normal state and oriented at two opposite critical angles to the plane of polarization of the light. The third field below is a photomicrograph of the point of irradiation, and it can be seen that at the exact point where the beam struck, the molecular arrangement of the multilayer is completely destroyed. Surrounding this point, a new orientation has sprung up. A similarity may be observed in the protein material of the nerve cell or the neurone axis cylinder, but even more strongly optically active in the living nerve cell is the myelin sheath which surrounds the neurone. The myelin substance is strongly birefringent, and is known to consist of lipoid molecules with their molecular axes oriented at 90° to the long axis of the neurone. At the junction of the axis cylinder and the myelin, there is one lipoid protein interface, and on the outside of the nerve sheath, there is another. This structure is quite susceptible to injury from radiation. Figure 26 shows myelinated tracts in the brain of an experimental animal exposed to 1,200 r of 550 kv. radiation. In this figure, on the right is seen a field from normal, unirradiated

hemisphere showing several myelinated fibers, and on the left a similar field, taken from an identical spot in the opposite hemisphere, which was exposed to radiation. It can be seen that, although the cytoarchitectural structure remains intact, the myelin sheath has lost a great deal of its optical activity.

During the past several years we have been investigating the effects of roentgen radiation on normal brain tissue, using dogs for experimental animals. Very briefly we may review this work by saying that it was shown that the myelin was rather sensitive to the radiation. The cells of the brain, being a non-proliferating type of cell, were expected to be radioresistant, and this proved to be the case, to about the degree expected. The ease with which we obtained myelin damage, however, gave the brain as a whole considerably more radiosensitivity than was to be predicted on the basis of the old belief that the brain is highly resistant to irradiation.

The myelin of the brain we now know to be made up of multilayers of protein and lipoid molecules arranged in a very precisely oriented structure. As is to be expected, this structure has strong optical activity, and may easily be studied in polarized light. We found that there were a number of advantages in the use of polarized light, either as an adjunct to the regular staining methods, or sometimes in preference to them. Staining methods require the complete dehydration and defatting of the specimen and in this series of radical chemical operations some of the brain structures are quite completely changed. In the polarized light method of observation, the specimen is not treated with any chemicals. In addition, we found that brain damage began when the myelinated nerves lost their optical activity, even though they retained their outward physical form. This phenomenon is illustrated in Figure 27, which shows, on the right a field in the irradiated area of a dog's brain and, on the left, a field from an identical area in the opposite hemisphere

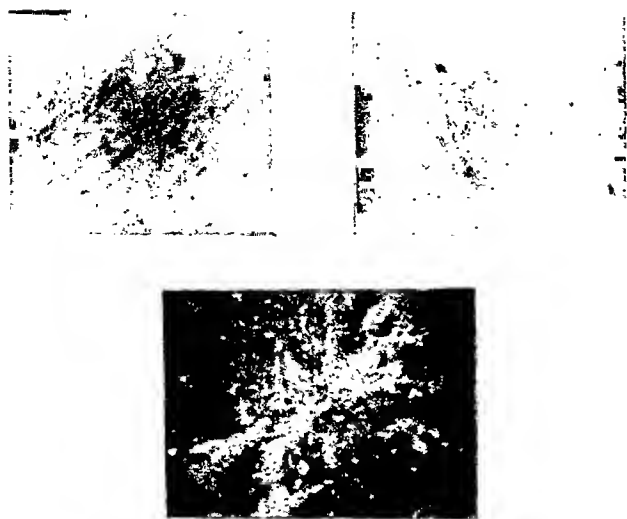


FIG. 25

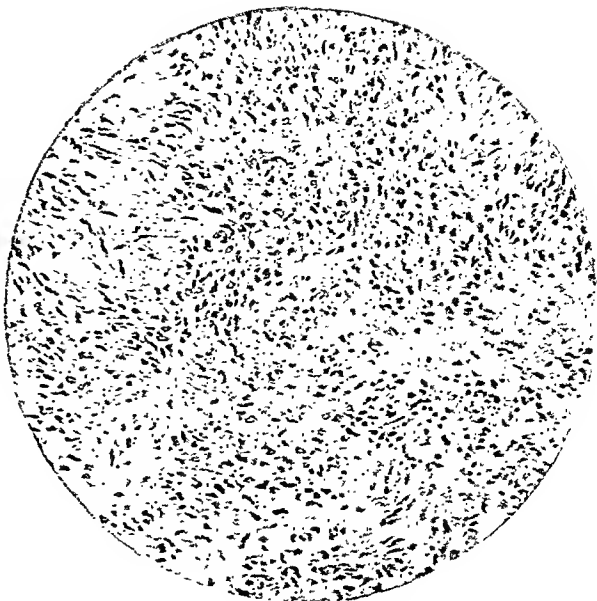


FIG. 28

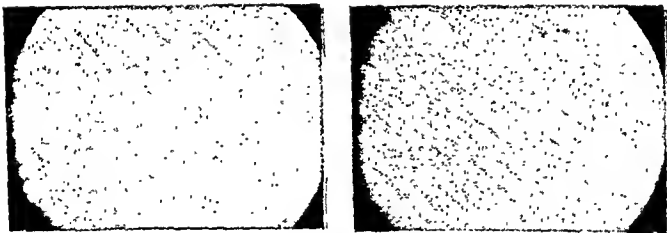


FIG. 26

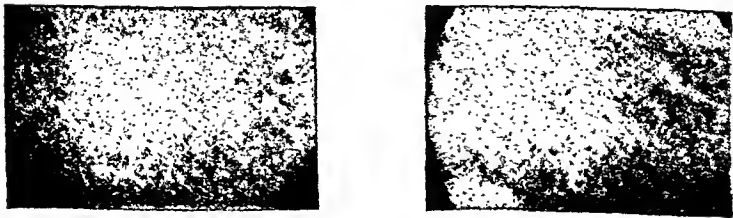


FIG. 27

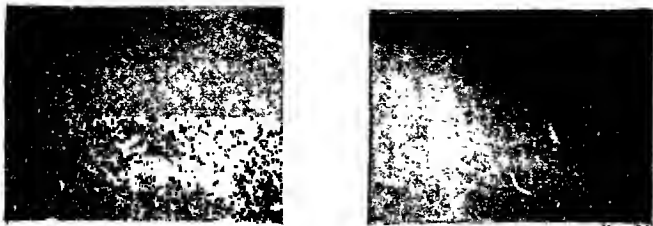


FIG. 29

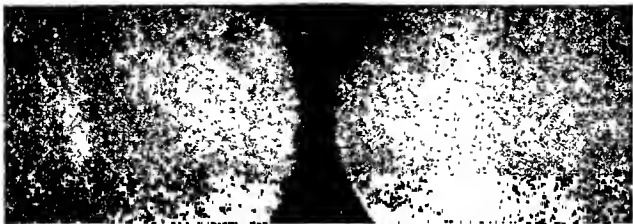


FIG. 30

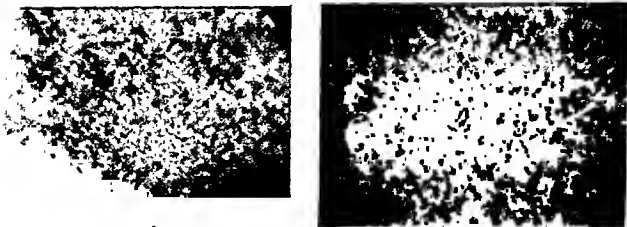
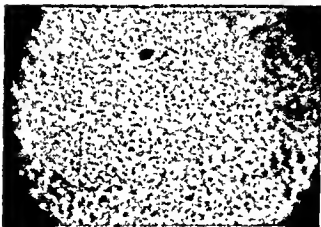


FIG. 31

of the brain of the same dog. The myelin is "stained" with the bright blue-green light of its own interference color in the polarized field of the petrographic microscope. In the irradiated area, the ability of the myelin to influence the polarized light is greatly reduced.

When we apply this method to the study of the human brain, we face certain complicating factors, due to the fact that we are dealing with a diseased brain. Some of the features observed in radiation damage are also seen in damage caused by pressure and diminished blood supply in a brain invaded by a malignant tumor; for example, in either case we find the disruption of the gross structure due to edema, and peeling of the myelin with formation of myelin ovoids. The following case, however, demonstrates that their radiation effect on the myelin can be distinguished even in the presence of complicating factors.

The patient had a deep-seated tumor (glioma) in the left temporal region which Dr. Schrieber, the neurological surgeon, considered inoperable. Two courses of high voltage radiation therapy were administered. Following the first series, the patient made a marked temporary improvement and returned to work. Four months later, he suffered a return of symptoms and was again given radiation therapy. There was no response to this treatment, and at autopsy an extensive infiltrating glioma was found. Figure 28 shows the histopathological appearance of the tumor at this time. Figure 29 shows the appearance of the myelinated tracts in the uninvaded hemisphere, in polarized lights. It can be seen at once that the myelin has assumed what we call, for lack of a better term, a "moth-eaten" appearance. It has lost optical activity in spots along the length of the fibers.

The second case is also an example of myelin degeneration. At operation, this patient had a large vascular glioma in the left temporal region. It was impossible to completely enucleate the tumor, and the patient was referred for radiation therapy.

Three series of radiation treatments were given. Following the first course, the patient showed marked improvement and returned to work. Four years later, he had a marked return of symptoms, and the tumor at this time was not responsive to treatment. The patient came to autopsy, and sections were taken both from the tumor and from the brain tissue of the opposite hemisphere. The histopathological appearance of the tumor at this time was the same as that shown in the preceding case.

Myelin damage of the type demonstrated in our experimental animals is shown to be present in the remaining normal brain tissue, which is shown in Figure 30. This is the outstanding example of this type of myelin degeneration that we have been able to obtain in human material up to this time. The myelin degeneration which follows radiation injury may take as much as a year to develop in an experimental animal. For purposes of rough comparison, we say that a dog lives six to seven times as fast as a man. It is interesting to consider in this connection that after four years the white matter tracts in the cerebral hemisphere opposite to the tumor had changed in this patient to a state in which, although their outward appearance was little changed, their optical activity had completely disappeared. This is shown in the upper two frames of Figure 30. These two fields may be compared to the lower frame, which is taken from normal brain tissue.

Figure 31 is an irradiated case which was a recurrent meningioma, rather than a glioma. The upper field shows the brain at a junction between white and gray matter, with the entire area infiltrated with compound granular fat cells. The two lower frames are of one field in the white matter. The specimen was rotated 90° on the stage of the microscope to show both of its interference colors in the beam of polarized light. The optical activity of the myelin is greatly reduced.

The important point in all of these cases

is the fact that the structures which depend for their functional properties on a highly organized system of polar molecules, the oriented lipoprotein layers of the myelin or the monolayers of the cell membranes, lose their organized structure and their optical activity when they are bombarded with high energy radiation. From animal experiments, we know that when the structural organization is gone, function is gone with it, and forever.

In the course of these considerations, I have tried to show one of the directions along which modern research is leading us. What we know as modern clinical medicine today could not come into existence until the cellular structure of the body and of invading organisms was thoroughly understood. In the application of chemical drugs we use compounds which affect the cells. It is only within the last few years that anyone has been particularly interested in the precise manner in which the cells are affected, but today we consider it of the greatest importance to know whether a drug acts by chemically tying up some part of the cell structure, by interfering with the oxygen metabolism of the cell, or by some other and more devious means. In applying roentgen radiation as a therapeutic agent, we are making use of a powerful medium which can only exert its force on the cell structure of the body by taking disruptive and destructive action against the submicroscopic structures of which those cells are composed. By the study of this agent and its action, coupled with the appropriate physical and chemical studies from which it cannot logically be separated, we may come to know these submicroscopic structures as well as today we know the cells. We cannot predict precisely to what point these researches will lead us in practical clinical medicine any more than the early workers in histology could predict the clinical medicine and radiology of today, but just as the

elucidation of cell structure was the great foundation of the past, so in all probability is the study of submicroscopic structure the great research of today.

The radiologist may not make any contributions to these fundamental observations, but his practical mind leads him to experiment with and use them, and out of such use may come results which will be beneficial.

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SKELETAL AND PULMONARY METASTASES FROM CANCER OF THE KIDNEY, PROSTATE AND BLADDER

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THE literature contains few references to the subject of pulmonary metastases from cancer of the kidney, prostate and bladder, but it is abundant on skeletal metastases from these malignancies. The earliest reports, although they established the existence of these metastases, are not correct as to their incidence. This is understandable since the findings were based on postmortem material and many sites of spread of the primary tumor must have been overlooked. Later reports depended on roentgen findings, before the roentgen ray had reached its present technical excellence, and are probably inaccurate. Communications in the more recent literature are not subject to the above criticisms, but the total of cases reported are too few for exact figures as to the incidence of these metastases.

This paper has been written in the hope that the addition of our material may help clarify questions that still exist as to the frequency of these involvements. The patients at the Montefiore Hospital for Chronic Diseases were especially suitable for this investigation. The majority reached the hospital in the late stages of the disease and, in almost all instances, careful workup was possible before death. In addition, a large percentage also had postmortem examination. In order to obtain the most accurate picture possible of these extensions, only patients who died were included in this study. In this way we were able to visualize all phases of metastatic growth.

SKELETAL METASTASES

Kidney. Eighty-seven cases of carcinoma of the kidney were studied. Since the differentiation of hypernephroma from vascular carcinoma with clear cells is

frequently difficult, no attempt was made to separate them and they were grouped together. With few exceptions, however, the neoplasms were hypernephromas. In 39 instances (45 per cent) roentgen or post-mortem examination revealed skeletal metastases (Fig. 1).

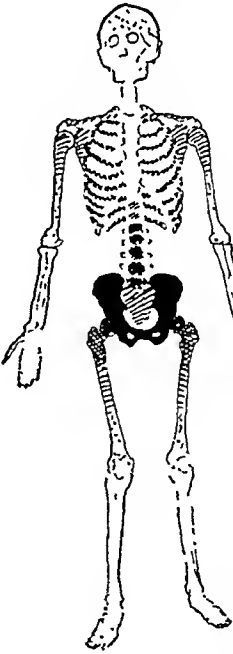
Albrecht,¹ in 1905, and Gottesman and co-authors,^{20*} in 1932, reported skeletal metastases in nearly half of their cases.

MALIGNANT TUMORS OF THE KIDNEY

Number of Cases	87
Cases With Skeletal Metastases	39 - 45%

ANATOMICAL DISTRIBUTION

Localization	No. of Cases	Percent.
Pelvis	18	48
Spine	15	38
Cervical 1		
Dorsal 8		
Lumbar 13		
Sacral 4		
Femur	14	36
Ribs	13	33
Scapula	9	23
Clavicle	7	18
Skull	6	15
Humerus	5	13



- 1. The metastases were generally multiple.
- 2. In 17 cases (45%) the metastases were confined to a single bone.
- 3. Type
 - A. Osteoclastic, occasionally with cystic changes.
 - B. Osteoblastic changes also occasionally present.

FIG. 1.

Copeland,¹² however, found the incidence to be 34.9 per cent, and Turner and Jaffe³⁹ reported only 20 per cent. Other authors

* Dr. Gottesman analyzed much of the material at the Montefiore Hospital up to 1932, and some of his cases have been included in the present report.



FIG. 2. Case I. Metastases to the right humerus from hypernephroma. Soft tissue swelling, extensive bone destruction and pathological fracture of the proximal portion of the right humerus.

have described bone involvement from kidney tumors but do not give percentages. These figures would certainly indicate a marked predilection for bone metastases from hypernephroma.

The anatomical distribution of the metastases is given in Figure 1. This shows the axial and trunk bones to be more frequently involved than are the bones of the limbs. With some exceptions, this corresponds rather closely to the findings of Copeland,¹² Sutherland and co-authors,³⁷ and Schinz and Uehlinger.³³ Pathological fractures are not infrequent and were observed in 7 instances, 5 in the femur and 2 in the humerus. Whereas skeletal metastases from tumors which have a predilection for bone are often multiple, this is not always the case with hypernephroma. In 17 instances, 43 per cent of the group, the lesions were confined to a single bone and to a single area in that bone. Schinz and Uehlinger³³ reported single metastases in 6 out of 20.

Frequently the kidney tumor is silent, and metastasis to bone is the first indication of the presence of a malignant growth. In some of these patients the roentgen appearance simulates a primary bone tumor. Attention was first focussed on such cases by Albrecht¹ in 1905. Scudder,³⁴ in 1906, Halstead,²⁴ in 1907, Gibson and Bloodgood¹⁸ and Joll,²⁶ in 1923, Gottesman and co-authors,²⁰ in 1932, and others have stressed this feature. Two illustrative reports follow:

CASE I (Hospital No. 28453). M.P., female, aged sixty-nine, had severe pain in the right arm, of six months' duration. She was treated for neuritis by several physicians before a diagnosis of a bone growth was finally made and she was referred to Montefiore Hospital. On admission, she presented a tender fusiform swelling of the upper third of the right humerus. Roentgen examination of this area showed soft tissue swelling, extensive bone destruction, and a pathological fracture of the upper third of the right humerus (Fig. 2). Except for a slight secondary anemia, all laboratory examinations, including the Bence-Jones test, were negative. High voltage roentgen therapy to the involved area was followed by disappearance of the soft tissue swelling and marked relief of pain. A few months later, metastases appeared in the pelvis, upper right femur, lungs and pleura. The postmortem examination revealed a small,



FIG. 3. Case II. Metastases to the pelvis and right femur from hypernephroma. There is extensive bone destruction of the right ilium, ischium, pubis and head of the right femur. The lesion has some resemblance to a multilocular cyst.

silent hypernephroma in the left kidney with metastases to the lungs, pleura, pericardium and suprarenal glands.

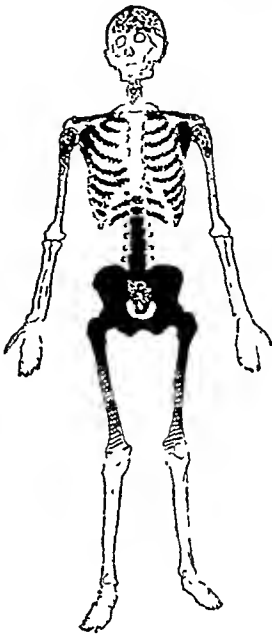
CASE II (Hospital No. 15824). C.F., male, aged seventy-one, sought treatment for pain localized to the right groin and buttock. He was first told he had rheumatism. Later, roentgenograms were taken and the diagnosis changed to Paget's disease. Pain persisted, and the right upper thigh became swollen and a large, deep, fixed mass could be palpated in the right lower quadrant. He was re-examined; a diagnosis was made of giant cell tumor of the pelvis and he was referred to Montefiore Hospital for radiotherapy. Roentgenograms now revealed, in addition to Paget's disease of the pelvic bones, marked destruction of the right ilium and sacrum (Fig. 3). The extensiveness and osteolytic character of the lesion, and the fact that no other bones were involved, caused us to make a tentative diagnosis of metastatic hypernephroma. A kidney tumor, however, could not be demonstrated. He was given intensive radiotherapy with partial relief of pain. Fifteen months later, biopsy at another institution, was positive for hypernephroma.

Roentgen Characteristics. The lesions may be multiple or single. They are always destructive in character and rarely produce new bone. The earliest sign is an area of

rarefaction in the medullary portion of the bone. As the growth progresses, the cortex may expand. At times, the external appearance is that of a simple cyst produced by the metastasis breaking through the

PROSTATIC CARCINOMA.

Number of Cases	60
Cases with Skeletal Metastases	35 - 58%



ANATOMICAL DISTRIBUTION

Localization	No. of Cases	Percent
Pelvis	26	74
Spine	Cervical 2 Dorsal 14 Lumbar 21 Sacral 5	68
Femur	20	57
Ribs	18	51
Scapula	14	40
Clavicle	10	28
Humerus	7	20
Skull	7	20
Mandible	1	3
Tibia	1	3

1. The metastases were generally multiple.
2. Type
A. Predominantly osteoblastic.
B. Only three cases were purely osteoclastic in character.

FIG. 5.

cortex of the bone, with the formation of local cystic growths, occasionally pulsatile (Fig. 4). The metastases have a predilection for the upper ends of the long bones, the regions of the nutrient vessels. It is noteworthy that when the pelvis is involved, the upper third of the femora frequently has lesions. Geschickter and Copeland¹⁷ have noted, and it is also our impression, that the small silent hypernephromas give rise to more extensive bone involvement than the larger kidney growths. However, we believe this to be due to the fact that the small silent lesions are not as fulminating as the larger growths and therefore the survival period is greater in the former group.

Prostate. The first recorded case of skeletal metastases from carcinoma of the prostate was by Thompson,³⁸ in 1854. However, very little was known of these



FIG. 4. Atypical metastasis to the skull from hypernephroma. The metastasis has broken through the internal and external plates of the frontal and parietal bones to produce a swelling which on palpation felt like a cyst. Vertical new bone formation extends into the mass.

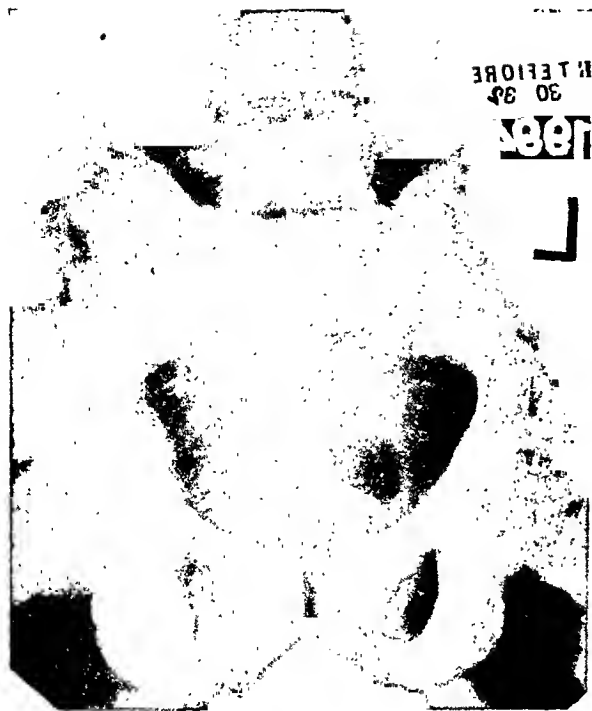


FIG. 6. Osteoplastic metastases from carcinoma of the prostate. Extensive laying down of new bone in the lumbar spine, pelvis and femora.

metastases until von Recklinghausen,³² in 1891, published the first complete work on this subject. More recently, the contributions in this field have been frequent and of great interest.

We investigated 60 patients with carcinoma of the prostate and in 35 (58 per cent) there were found skeletal metastases

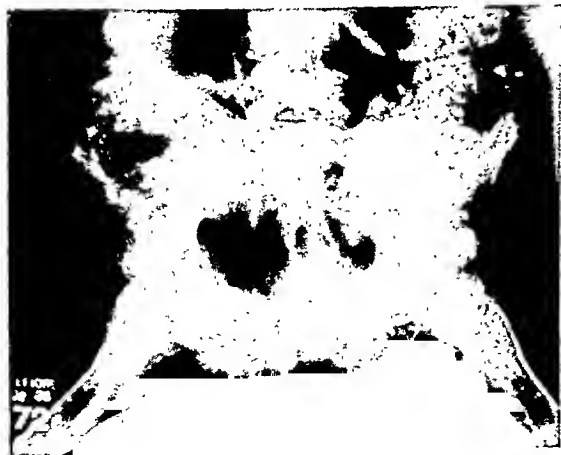


FIG. 7. Metastases from carcinoma of the prostate. In contrast to Figure 6, the metastases appear as small islands of dense bone. Superficially there is some resemblance to osteopoikilosis.

(Fig. 5). Bumpus,⁷ in 1921, reported skeletal involvement in 41 patients (30 per cent) out of 135 with roentgen examination. Copeland,¹² in 1931, studied 1,040 cases. Only 50 per cent of these had roentgen studies and of this number, 25 per cent were positive. Sutherland,³⁷ in 1932, found the bones positive in 296 (28.6 per cent) of the patients examined. Our figures are identical with those of Turner and Jaffe,³⁹ who reported involvement in 57.8 per



FIG. 8. Osteoclastic metastasis from carcinoma of the prostate. Areas of bone destruction with no evidence of new bone formation are present in both femora and both ilia.

cent of 95 autopsies. Among the highest figures are those of Kaufmann,²⁷ who reports a small group of 24, in 16 (67 per cent) of whom there were skeletal metastases. We found the pelvis, spine, femur, ribs, scapula, clavicles, humerus and skull, in the order named, the bones most frequently involved.

As with kidney tumors, the lesions in the bones may be the first indication of a malignant growth.

Roentgen Characteristics. The metastases are essentially osteoplastic in character, but small areas of bone destruction are also generally present (Fig. 6). Rarely, the metastases present themselves as small areas of dense bone, of varying size, scattered throughout the marrow spaces (Fig. 7). In only 3 instances were purely osteoclastic changes observed (Fig. 8).

The osteoplastic nature of these metastases has been the subject of study by a number of authors. Recklinghausen³² has described the histopathological process as a carcinomatous osteitis. The tumor cells lodge in the capillaries and venules, cause stasis and hemorrhage, which is then followed by reactive growth of osteoid and, finally, osseous tissue. Goetsch¹⁹ and Axhausen² believe that some unknown chemical irritant emanating from the tumor cells acts on the old bone and stimulates proliferation. Others state that the invasive powers of the metastatic tumor are so moderate that proliferation of bone keeps up with destruction by the tumor. The recent work in the field of serum phosphatase gives new weight to the latter theory. Gutman, Sproul and Gutman²³ have shown strikingly increased phosphatase activity of bone at the site of osteoplastic skeletal metastases in a patient with carcinoma of the prostate gland. This observation is in accord with the view, derived from pathological studies, that the mechanism of bone formation in metastatic osteoplastic neoplasms is fundamentally the same as that of normal bone formation.

Bladder. The literature on the subject of skeletal metastases from carcinoma of the bladder is both vague and limited. The earliest reports consisted of isolated cases (Clutton,¹¹ Wells,⁴⁰ Pic *et al.*,³¹ Christensen,¹⁰ Livingston³⁰). In 1922, Kretschmer²⁹ reported 3 cases, Sutherland *et al.*,³⁷ in 1932, 9 cases, Graves and Militzer,²¹ in 1934, 5 cases, Greenfield,²² in 1941, 3 cases, and Herger and Sauer,²⁵ in 1942, 4 cases. The Carcinoma Registry of the American Urological Association⁸ published 902 epithelial tumors of the bladder. Metastases were found in 72, or 8 per cent. Of the latter number, the bones were involved in 34. If we consider the original group of 902, the skeleton was positive in 3 per cent of the cases. The bones most frequently involved were the lumbar spine, pelvis and femora, in the order stated.

Spooner,³⁶ on the other hand, in 1934, in

a review of the material from the Mayo Clinic from 1914 to 1931, inclusive, found invasion of the bone, except by direct extension, to be an uncommon feature. This is also true of the material from the Johns Hopkins Hospital reported by Cope-land¹² in 1931, and of the material from the Montefiore Hospital. In our group, bone involvement was present in 6 cases but in

CARCINOMA OF THE BLADDER

Number of Cases 56

Cases With Skeletal Involvement 6 - 10%

ANATOMICAL DISTRIBUTION

Localization	No. of Cases	Percent
Pelvis	4	66
Femur	1	17
Sacrum	1	17

1. Type Osteoclastic.

2. With the exception of the femur, the involvement was by extension in all cases.

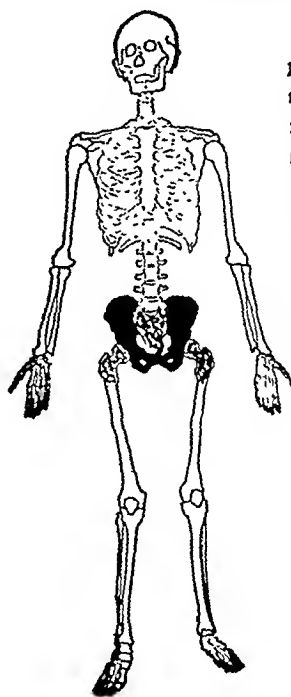


FIG. 9.

only 1 instance were true metastases observed (Fig. 9). In the other cases, the pelvis was invaded by direct extension from the primary tumor.

From what has been written on this subject, one can therefore conclude that skeletal metastases from carcinoma of the bladder, while infrequent, do occur. In the cases cited from the literature, the involvement was practically always osteoclastic.

Therapy. Our experience with skeletal metastases from carcinoma of the bladder is so limited that this discussion will be confined to the radiotherapy of bony

extensions from carcinoma of the prostate and kidney. To properly plan treatment, it is necessary to consider both the extent of the lesions and the stage of the disease. If the metastases are widespread, the treatment is limited to the sites causing symptoms, or to areas where fracture of the bone is impending. Where visceral me-

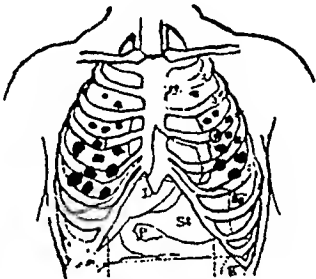
present, some new bone may be laid down. In patients with hypernephroma, if the metastases respond to treatment, the area of destruction shows little change, otherwise it may increase in size.

Whereas in breast metastases, symptomatic relief and healing of bone can often be accomplished by moderate dosage, this

MALIGNANT TUMORS OF THE KIDNEY

Pulmonary And Pleural Metastases.

Total Number Of Cases	87
Total Number Of Postmortems	59
Total Number Of Pul. or Pl. Met.	47 - (31 Verified at P.M. 54% (16 Diag. Only by X-ray.



Postmortem Findings In Lungs

- 1. Nodular parenchymal lesions most frequent.
- 2. Next in frequency, positive hilar nodes and nodules in lungs and pleura.
- 3. Then, positive hilar nodes and lymphangitic metastases to lungs and pleura.

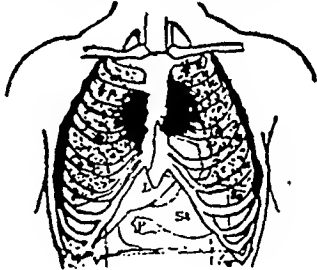
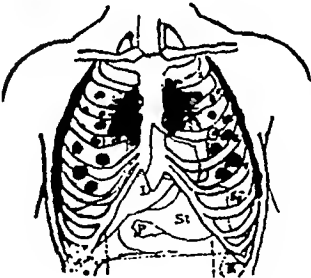


FIG. 10.

tastases are also present, this palliation is the entire therapeutic aim. On the other hand, if the metastases are few in number, as in hypernephroma, intensive treatment is advisable to achieve more lasting control of clinical symptoms.

Contrary to our experience in treating skeletal metastases from cancer of the breast, little if any healing of bone follows the irradiation of these lesions. The improvement that takes place is almost entirely relief of pain. In prostatic cases, the osteoplastic appearance of the bone is generally not altered; if destruction is

is rarely so with kidney and prostate cases. These patients usually require intensive treatment with high voltage, with total dosages of 2,000 to 3,000 r per field over one or more fields, to control pain.

PULMONARY METASTASES

In contradistinction to the voluminous literature on the frequency and character of skeletal metastases from cancer of the genitourinary tract, little mention is made of the pulmonary spread from these tumors. The incidence of pulmonary involvement in our group, and comparison

with some of the reports in the literature, should therefore be of interest to roentgenologists and urologists.

Kidney. Albrecht¹ found the lungs involved in all his advanced cases of renal cancer. Willis⁴¹ states that it occurs in 75 per cent of kidney neoplasms. Albarron,¹⁴ however, reporting on 249 cases, discovered pulmonary metastases in only 75, or 30 per cent. Recently Turner and Jaffe³⁹ reported pulmonary metastases in 40 per cent of 25 autopsies.

We investigated 87 cases and found



FIG. 11. Parenchymal and pleural metastases from carcinoma of the kidney. Large nodular metastases are scattered throughout both lungs, most numerous at the bases. A small effusion is present on the left side.

pulmonary or pleural metastases present in 47, or 54 per cent (Fig. 10).

For purposes of classification, the lesions have been divided into those of the parenchyma, pleura, and mediastinal or hilar lymph nodes. The parenchymal lesions were by far the most frequent. They usually consisted of fairly large, sharply outlined nodules, most numerous in the lower two-thirds of the lungs (Fig. 11). Widespread miliary lesions were also seen (Fig. 12), and occasionally enlarged mediastinal and hilar nodes were observed (Fig. 13). In some instances, the tumor broke through the gland capsules and infiltrated the lung, giving a roentgen ap-



FIG. 12. Widespread miliary metastases from carcinoma of the kidney. Postmortem examination showed miliary distribution of tumor nodules throughout both lungs. The streak-like shadows extending out from the hilar areas were due to lymphatics filled with tumor cells. The hilar nodes were enlarged and invaded by the neoplasm.

pearance suggesting a primary cancer of the bronchus (Fig. 14). Predominantly pleural involvement was not often present; when seen, there was also usually an associated pleural effusion (Fig. 15).

Prostate. Cancer of the prostate gives rise to pulmonary metastases less frequently than hypernephroma. In a group of 22 cases, Kaufman²⁸ reported the lungs



FIG. 13. Metastases to mediastinal and hilar lymph nodes from carcinoma of the kidney. The appearance suggests lymphoblastoma. The postmortem examination also showed a few small tumor nodules at the right base.



FIG. 14. Metastases to the lungs, mediastinal and hilar lymph nodes from carcinoma of the kidney. The appearance is suggestive of carcinoma of the lung. Postmortem examination showed neoplastic masses in both hilar regions. From these areas there radiated a series of small tumor nodules, particularly along the course of the bronchi and in the upper lobes.

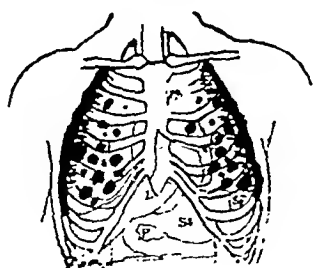


FIG. 15. Pulmonary and pleural metastases from carcinoma of the kidney. Postmortem examination showed infiltration of the pleura of both lungs with carcinoma. The lymph vessels of the lungs, also the hilar nodes, were invaded by neoplasm.

CARCINOMA OF THE PROSTATE

Pulmonary And Pleural Metastases.

Total Number Of Cases	60
Total Number Of Postmortems	39
Total Number Of Pul. or Pl. Met.	26 - { 20 Verified at P.M. 43% { 6 Diag. Only by X-ray.



Postmortem Findings In Lungs

1. Nodules in pleura and lungs most frequent.
2. Next in frequency, nodular parenchymal lesions, occasionally lymphangitic in type.
3. In a few cases, only hilar nodes were involved.
4. Pulmonary lymphatics were frequently invaded.

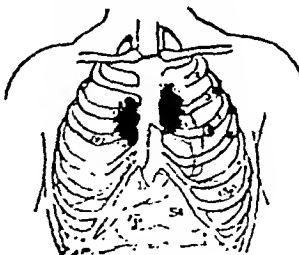
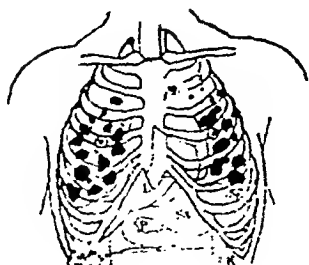


FIG. 16.

involved in 40 per cent and the pleura in 58 per cent. Willis⁴¹ found pulmonary involvement in 35 per cent and Turner and Jaffe³⁹ in only 28.4 per cent of 95 autopsies.

In this group, 26 cases (43 per cent) had intrathoracic extension of the disease (Fig. 16). At postmortem, the most frequent finding was the association of pleural and pulmonary metastases. In these patients, the pleura was either studded with nodules or else diffusely infiltrated (Fig. 17). The pulmonary lesions consisted of subpleural infiltrations and nodules scattered throughout the lungs. Pleural effusions were common in this group. Next in frequency were parenchymal lesions, consisting either of numerous nodules, pea-sized to miliary, or else a few large circular masses. Rarely only a single nodule was found. At times, the involvement was predominantly hilar, with extension therefrom into the lower lobes of both lungs. Pleural lesions were also occasionally present with this type. In a few instances, the lungs appeared

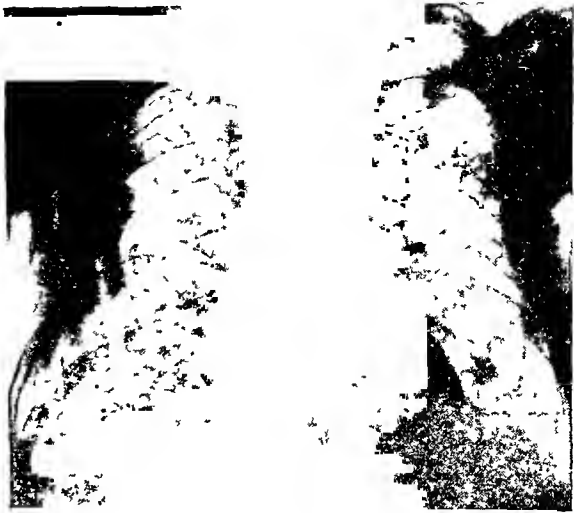


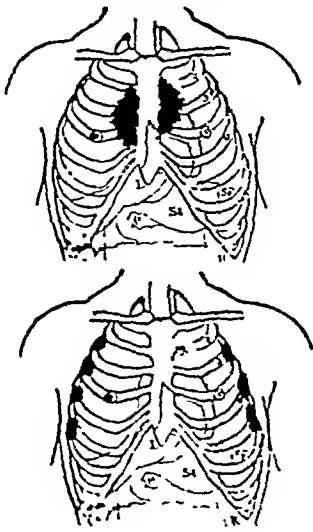
FIG. 17. Pleural metastasis from carcinoma of the prostate. The metastasis appears as a scalloped shadow along the periphery of the left pulmonary field (arrow). The left infraclavicular shadow is due to a rib metastasis.

negative macroscopically but microscopic sections showed invasion by tumor cells of the parenchyma or peribronchial lymphatics.

CARCINOMA OF THE BLADDER

Pulmonary And Pleural Metastases.

Total Number Of Cases	56
Total Number of Postmortems	35
Total Number Of Cases With	
Intrathoracic Involvement	4 - 7% (All Verified at P.M.)



Postmortem Findings In Chest

1. Metast. to mediast. glands in one patient.
2. Metast. to hilar nodes. Tumor cells in capillaries, veins and lymphatics.
3. Few small subpleural nodules in another patient.
4. Tumor cells found in one instance in a thrombus in an artery of the lung.

FIG. 18.

Bladder. The literature is most confusing on the frequency of pulmonary metastases from cancer of the bladder. Barringer³ and Kaufman²⁸ state that such extensions are rare. Geraghty,¹⁶ on the other hand, states that the lungs are a favorite site for these metastases. Spooner,³⁶ in his analysis previously referred to, reported pulmonary extension in 9 cases, or 5 per cent. The Carcinoma Registry of the American Urological Association⁸ found 11 cases (14 per cent) of metastases to the lungs in 79 postmortem examinations. Turner and Jaffe³⁹ report 19.5 per cent involvement in 46 postmortems.

In this series, 4 cases, or 7 per cent, showed intrathoracic involvement (Fig. 18). Two patients had metastases to the mediastinal or hilar nodes, 1 patient presented a few small subpleural nodules and in the last case, tumor cells were found in a thrombus in an artery of the lung. In these patients, the tumor had extended outside the bladder to involve the regional glands.

Symptoms. Cough and dyspnea are the two complaints most commonly encountered when pulmonary involvement is present. Pain occurs next in frequency. Hemoptysis rarely presents itself as a symptom. In a small number of patients, physical signs, such as dullness, diminished breath sounds and râles, are the first indication of pulmonary metastases. If the pulmonary involvement is slight, no symptoms or physical signs may be present and the lesions are then discovered only on roentgen or postmortem examination.

When the predominant lesion is parenchymal, as in the case of hypernephroma, cough is the most frequent symptom. Where the pleura is most frequently involved, as in prostatic carcinoma, dyspnea due to pleural effusions, and pain are the earliest manifestations of the intrathoracic involvement.

Mode of Spread of Metastases. The kidney has a very rich vascular supply and early invasion of the blood stream by cancer is frequent. It is therefore to be expected that

pulmonary metastases from kidney malignancies should be embolic by way of the blood stream. The predominance of parenchymal lesions bears this out. The postmortem material also shows that pulmonary involvement occurs by lymphatic permeation through the diaphragm and on to the parietal pleura, and by way of emboli along lymphatic channels.

The frequency of both pleural and parenchymal involvement from cancer of the prostate suggests invasion by both lymphatic and hematogenous routes. The prostate is richly supplied with lymphatics. Extension takes place by way of the regional nodes to the mesenteric and retroperitoneal nodes, thence to the thoracic nodes and then retrograde to the lung and pleura along the smaller lymphatics.

Effect of Radiotherapy. Irradiation is often ineffectual with pulmonary metastases from cancer of the urinary tract. Lung involvement is frequently a terminal affair and is usually associated with metastases to other viscera. The patients are in such poor general condition that they cannot tolerate the large doses of radiation necessary for relief of symptoms. Occasionally, however, relief of cough and dyspnea and, when pleural effusions are present, slower refilling of the chest will follow such treatment.

CONCLUSIONS

1. Skeletal and pulmonary metastases were investigated, either by roentgen or postmortem examinations, in 203 patients who died from cancer of the kidney, prostate and bladder.

2. Of 87 patients with cancer of the kidney, 39 cases, or 45 per cent, revealed skeletal metastases. In 47 instances, or 54 per cent, pulmonary, pleural or mediastinal metastases were also present.

3. Sixty patients with cancer of the prostate were investigated. In 35 cases, or 58 per cent, skeletal metastases were found. Pulmonary, pleural or mediastinal involvement was discovered in 26 cases, or 43 per cent.

4. Of 56 patients with cancer of the bladder, bone involvement was present in 6 cases, or 10 per cent, but in only one instance were true metastases observed. In the other cases, the pelvis was invaded by direct extension from the primary tumor. In this series, 4 cases, or 7 per cent, showed intrathoracic involvement.

5. Intensive radiotherapy relieves pain in a large number of patients with skeletal metastases from cancer of the kidney and prostate.

6. Irradiation is often ineffectual in pulmonary metastases from cancer of the urinary tract. Occasionally, however, relief of cough and dyspnea and, when pleural effusions are present, slower refilling of the chest will follow such treatment.

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ABDOMINAL LYMPHOGRANULOMATOSIS

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ALTHOUGH enlargement of the superficial lymph nodes is the most spectacular aspect of Hodgkin's disease and the most frequent reason for the patient to seek medical attention, other manifestations of the disease have been the subject of investigations in recent years. For example, lymphomatous involvement of the pulmonary¹⁵ and osseous¹⁶ systems and of the breast¹ have been studied intensively in the past few years at the Memorial Hospital. Since approximately 15 per cent of the cases of Hodgkin's disease seen at this institution develop symptoms referable to the gastrointestinal tract at some period of the illness, it was thought that a study of the abdominal manifestations of this malady might be instructive.

Terplan¹⁴ divided cases of Hodgkin's disease of the gastrointestinal tract into those in which the digestive tract is exclusively involved and those in which it is involved as part of a generalized or disseminated process. This grouping does not include those cases in which there are gastrointestinal manifestations produced by extrinsic disease. Therefore the following classification is proposed.

1. Primary gastrointestinal lymphogranulomatosis.
2. Secondary gastrointestinal lymphogranulomatosis.
3. Extrinsic gastrointestinal lymphogranulomatosis.

The accurate differentiation of these three groups may sometimes be impossible by clinical means. In these instances the distinction can only be made by postmortem study.

PRIMARY LYMPHOGRANULOMATOSIS OF THE GASTROINTESTINAL TRACT

Attention to primary lymphogranulomatosis as a clinical entity was drawn by

Schlagenhauser¹¹ in 1913 when he described gastric lymphogranulomatosis without involvement of any other organ. Previous to this according to Terplan¹⁴ the localized form of lymphogranulomatosis was probably classified as sarcoma of the bowel or tuberculous enteritis. By 1927 Hayden and Apfelbach⁷ were able to collect 26 cases from the literature and to add 3 of their own. Singer,¹² in 1931, reviewed the literature and selected 6 cases which he concluded were unquestionable examples of primary gastric lymphogranulomatosis, in which no other focus of disease was demonstrable, and added 1 of his own. In 1936 Madding⁸ of the Mayo Clinic published a report on 6 cases of primary Hodgkin's disease of the stomach which had been seen over a period of the preceding eight years. Bini and Parvis,² in 1940, published a paper on primary lymphogranulomatosis of the gastrointestinal tract in which they reviewed the literature exhaustively. There were over a hundred references cited which represented about 150 cases.

Primary lymphogranulomatosis may involve any part of the gastrointestinal tract or several segments concomitantly; the stomach, however, appears to be the most frequent site. The symptomatology is dependent upon the portion of the digestive tract involved. The majority of the patients are in the fifth decade and males predominate in the ratio of 2 to 1.

Lymphogranulomatosis of the stomach may involve any portion of the organ. The pylorus, however, is the most frequent site. The presenting symptoms may be epigastric or abdominal pain relieved in some instances by food or alkalis, postprandial distress, nausea, vomiting, gaseous eructations and anorexia. There may be weakness, loss of weight and hematemesis. The process may produce pyloric obstruction with

its concomitant signs and symptoms.

Gastric analysis may show an achlorhydria but in many instances the gastric acidity is within normal limits. There may be a moderate secondary anemia. There is usually no significant alteration in the leukocytes with the exception of an occasional slight eosinophilia.

Physical examination is for the most part non-contributory. There may occasionally be some evidence of weight loss. A palpable mass in the abdomen is uncommon and the liver and spleen are usually not felt. Superficial lymphadenopathy and pyrexia are infrequent.

Roentgen studies may reveal a filling defect which is interpreted as being caused by a cancer or ulcer. When the roentgenologic and physical findings are correlated with the symptomatology the diagnosis in nearly all instances is neoplasm or ulcer, the former being the more frequent conclusion. The correct diagnosis is made at operation or autopsy.

The lesions, which are grayish or pearly white in color, may occur in any part of the stomach. They may be flat, nodular, or in some instances in the form of convolutions somewhat resembling those of the cerebrum. Macroscopically the disease appears as an infiltration with consequent thickening of the gastric wall. It may be limited to a small area or it may be diffuse throughout the whole organ producing an effect similar to linitis plastica. The lesion may be ulcerated and bear a resemblance to a neoplasm. The ulceration may give rise to perforation or to hemorrhage which on occasion may be severe enough to cause death. The adjacent lymph nodes may be large, discrete, soft and succulent.

The treatment for disease localized to the stomach is gastric resection. Involved omental nodes should be removed at the same time. In some of the cases reported from the Mayo Clinic in which involved omental nodes were removed at the resection, the patients were alive and apparently free from disease six to eight years later.

The incidence of this disease in the in-

testine is greatest in the upper part of the small bowel and decreases from there to the rectum. Involvement of the bowel may be characterized by malaise, weakness, abdominal pain, meteorism, diarrhea, constipation or alternating diarrhea and constipation. There may be irregular bouts of fever and occasionally a palpable abdominal or rectal mass. Superficial lymphadenopathy is infrequent. Often there is a secondary anemia and sometimes a leukopenia. With this symptomatology the condition may simulate typhoid fever. On the other hand, the clinical picture may be that of an acute obstruction or intussusception. There may be perforation with peritonitis or hemorrhage which may be fatal. The diagnosis is established at laparotomy. Surgical removal of the lesion relieves the symptoms and in numerous instances has apparently effected a cure.

SECONDARY LYMPHOGRANULOMATOSIS OF THE GASTROINTESTINAL TRACT

Secondary lymphogranulomatosis of the gastrointestinal tract occurs as part of the generalized disease process. Pitt¹⁰ in 1889 described lesions in the stomach and duodenum occurring under these circumstances. The patient may or may not complain of gastrointestinal symptoms and the lesion may be discovered only at postmortem examination. In a series of 295 deaths from Hodgkin's disease in cases followed at the Memorial Hospital during the decade of 1932 to 1942 there were 36 autopsies. Six, or 1.7 per cent, of these revealed, in association with the generalized disease, lesions of the gastrointestinal tract—5 in the stomach and 1 in the duodenum. The duodenal lesion was a healed ulcer whose base showed Hodgkin's disease on microscopic examination and it was assumed that the ulceration was secondary to the lymphogranulomatous process. This patient had gastric symptoms when first seen at the clinic. There was no ulcer history but a gastrointestinal roentgen examination was reported as suggestive of duodenal ulcer.

Of the 5 patients with gastric involve-

ment, 2 gave a history of epigastric pain, nausea and vomiting. In 1, a woman, roentgen studies revealed an irregularity in the prepyloric region where, at autopsy, a large superficial ulcer with slightly elevated edges was found. Microscopic examination revealed the ulcer to be, for the most part, nonspecific but to have minute specific lesions at its base. In the other patient, although the gastrointestinal series failed to reveal any abnormality, at autopsy a nodular excrescence was found in the fundus which was pronounced Hodgkin's disease on microscopic study. In addition, near the antrum, in an area free of Hodgkin's disease, was a punched out ulcer 3 cm. in diameter, which microscopically suggested an ulcerating cancer. It is of interest that the initial superficial lymph node in each of these cases appeared in the inguinal region and showed Hodgkin's disease on biopsy. In the 3 cases that had no gastric symptoms, nodular lesions, proved to be Hodgkin's disease by microscopic examination, were found at autopsy in the gastric wall. The sites of involvement were the pylorus, the posterior gastric wall and the greater curvature respectively. Thus it appears that intrinsic disease of the stomach may remain asymptomatic.

In another patient a diagnosis of secondary intrinsic disease of the stomach was established by gastroscopic examination.

This patient was an Italian woman, aged twenty-nine, who came to the clinic complaining of a swelling in the left side of the neck which appeared one year previously and had increased somewhat in size since its inception. Later she developed a dry non-productive cough. Examination was negative except for an indefinite swelling over the lower third of the left sternocleidomastoid muscle. Two small soft nodes were palpable near the swelling. A biopsy of one of these nodes was reported as Hodgkin's granuloma. A roentgenogram of the chest revealed a mediastinal mass displacing the trachea to the right. She received roentgen therapy to the left neck and mediastinum with marked regression of the lesions and she remained well, except for a small right supraclavicular node controlled by roentgen therapy, for a period of

two and a half years. At this time she developed gastric distress and diarrhea. A gastrointestinal roentgen examination revealed a slight saw-tooth appearance along the lesser curvature. A gastroscopy was performed at which a definite nodular and linear infiltration of the pars media and lesser curvature was seen as well as numerous punctate hemorrhages in the area of infiltration. The gastroscopist made a diagnosis of Hodgkin's disease involving the pars media of the stomach. High voltage roentgen therapy was administered to the stomach through an anterior and posterior field giving a dose of 1,200 r to each area. This was followed by a disappearance of the gastrointestinal symptoms, and at gastroscopy two months later no abnormality of the stomach was seen. With the exception of the appearance of a node in the right spinal accessory chain, the patient has remained well to date (five and a half years).

Secondary involvement of the gastrointestinal tract might be a more common occurrence if the individual did not succumb to the disease so early. The retroperitoneal nodes involved by this disease increase slowly in size over a long period of time and rarely demonstrate invasive characteristics. That this may occur, however, in the relatively long lived patient is illustrated by the following case:

This patient was a female, aged twenty-two, whose illness began in 1929 with enlargement of the left cervical lymph nodes followed by enlargement of those in the left axilla. An axillary and cervical node were removed at another institution and diagnosed as Hodgkin's disease following which she received five roentgen treatments to the neck and axilla over a period of seventeen months. She was then referred to the Memorial Hospital for further treatment. Examination in November, 1931, at this institution revealed enlarged nodes in the left neck, left supraclavicular region and in both axillae. In May, 1934, about five years after the onset of her illness, she began to develop severe pain in the right upper quadrant of the abdomen. No masses or organs were palpable. The pain subsided after several weeks and she remained asymptomatic for about one year.

In May, 1935, she returned with a complaint of severe upper abdominal pain which required sedatives for relief. Examination revealed a nodular mass in the left upper quadrant near

the midline which was interpreted as a group of lymph nodes. This area was irradiated, followed by subsidence of the mass and relief of the pain. However, the pain returned in a few months at which time a gastrointestinal roentgen examination was done and reported negative. Again there was a response of the pain to radiation therapy and an interval of freedom from discomfort.

For the next four years she had attacks of abdominal pain at intervals which were controlled by radiation therapy. During this period she also developed evidence of the disease in the mediastinum, lungs, pelvis and inguinal nodes and received roentgen therapy to these locations.

In 1941, twelve years after the onset of the disease, she developed lower abdominal cramps and diarrhea. Rectal examination revealed a firm, lobulated mass outside the rectal wall and posterior to it. Other masses were palpable throughout the lower abdomen. The intestinal symptoms continued as well as the abdominal pain and vomiting. Proctoscopic examination revealed a stenosis about 8 cm. up and grayish white thickened areas in this location. A biopsy of one of these lesions was diagnosed as Hodgkin's disease. A gastrointestinal series showed no evidence of intrinsic esophageal, gastric or duodenal disease. Radiation therapy was given to the rectal lesions but the patient's course was progressively retrogressive. She continued to have abdominal pain until her death a few months later. Her disease lasted thirteen years.

EXTRINSIC GASTROINTESTINAL LYMPHOGRANULOMATOSIS

In this group are the cases of Hodgkin's disease with gastrointestinal symptoms in which there is no clinical, roentgenographic or gastroscopic evidence of intrinsic gastrointestinal involvement but in which the symptoms are produced by extrinsic pressure of the enlarged abdominal lymph nodes. These are a continuation of the iliac chain and are divided into two groups: the mesenteric and the para-aortic. The nodes are connected by lymphatic vessels, the whole forming one closed system which empties into the left jugulosubclavian junction by means of the thoracic duct. The mesenteric nodes and lymph vessels follow the course of the blood vessels supplying

the abdominal organs. The lymphatics of the small bowel, large bowel and rectum consist of chains of nodes and vessels which follow the course of the superior and inferior mesenteric blood vessels. The stomach is drained by lymphatic channels and nodes on the greater and lesser curvatures which accompany the gastric and gastroepiploic arteries respectively. The pancreas and spleen are supplied with lymphatic vessels and nodes which follow the course of the splenic artery. In like manner, the liver and gallbladder are drained by nodes and lymph channels which accompany the hepatic artery, portal vein, cystic and common ducts and right gastroepiploic artery.

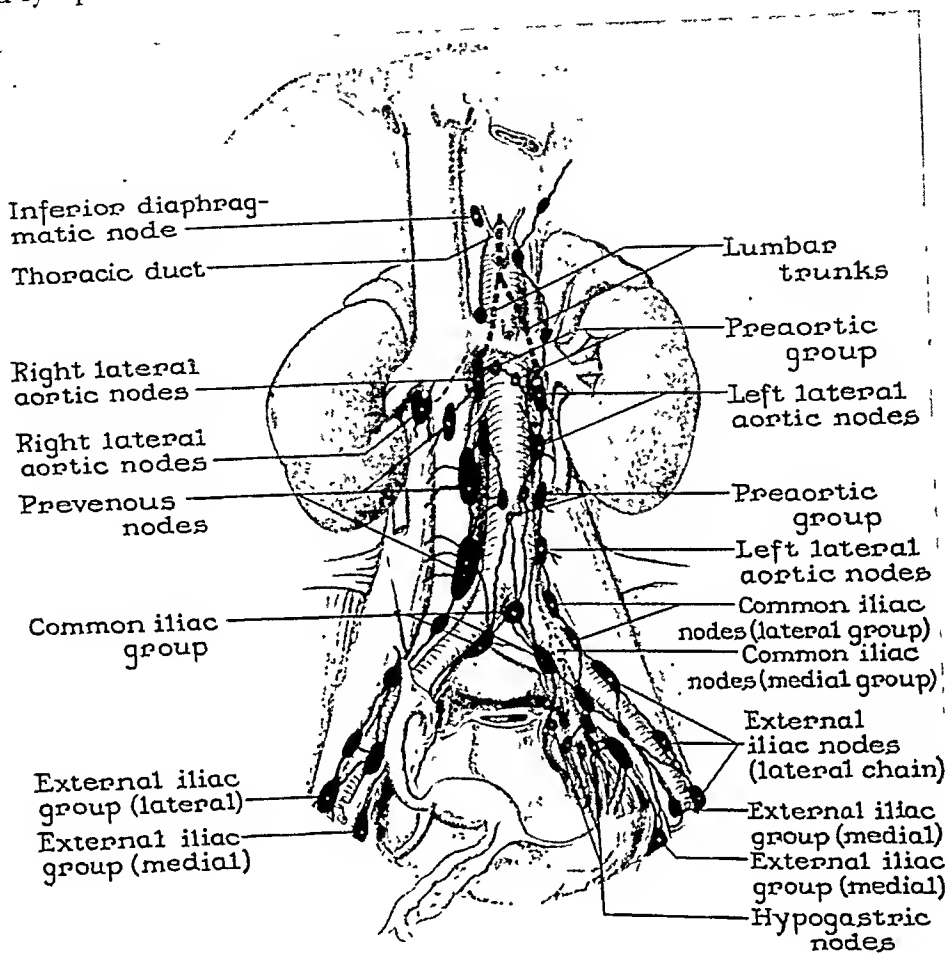
The mesenteric system communicates with the para-aortic nodes (Fig. 1). These consist of twenty-five or thirty large nodes which are distributed along the abdominal aorta and inferior vena cava, and surround these vessels. Some of the nodes lie in front, some behind, others to the right and left of the great vessels. There are groups of nodes at the origin of the superior and inferior mesenteric arteries and of the celiac axis. The mesenteric system of lymphatics accompanying these trunks empties into these respective groups.

From 1932 to 1942 inclusive a group of 406 cases of Hodgkin's disease, proved by biopsy, was seen at the Memorial Hospital. At the time of writing 295 are dead and 111 living. Of the entire group 52, or 12.8 per cent, developed gastrointestinal symptoms. Seven of these cases, of which 6 revealed specific gastrointestinal lesions at autopsy and 1 by gastroscopy, have been discussed under a previous heading. Hence there were 45 patients, or 11 per cent, in whom there was no clinical or roentgenographic evidence of intrinsic gastrointestinal involvement.

These figures are smaller than those of other investigators. Ziegler,¹⁷ for example, states that 35 per cent of the patients with Hodgkin's disease have gastrointestinal disturbances of which diarrhea is the most common symptom. Minot and Isaacs⁹ analyzed 477 cases of lymphoblastoma and

found that 25 per cent had as their initial symptom one referable to an abdominal lesion. No attempt was made to break down the grouped lymphoblastoma into its com-

ponents, or 71 per cent, was enlarged cervical lymph nodes. This figure is comparable with that given by Goldman⁶ for Hodgkin's disease as a whole. The frequency with



Abdomino-Aortic Lymph Nodes
(Schematic)

FIG. 1. Adapted from "Anatomy of the Human Lymphatic System" by Rouvière, translated by Tobias. Edwards Bros., Inc., Ann Arbor, Mich. 1938. (Reproduced by permission.)

ponent elements so that this figure is not comparable with the one we obtained for Hodgkin's disease.

The average age of the 52 patients developing gastrointestinal manifestations was thirty-six years. The number of males in this group was 39, or 75 per cent, and the number of females 13, or 25 per cent. These figures for average age and sex distribution correspond with those for Hodgkin's disease in general.

The initial complaint in 37 of the pa-

tients, or 71 per cent, was enlarged cervical lymph nodes. This figure is comparable with that given by Goldman⁶ for Hodgkin's disease as a whole. The frequency with

which the initial nodes occurred in the various sites is shown in Table I. The initial symptoms referable to the gastrointestinal tract were in most cases abdominal pain or epigastric distress. Some individuals, however, had diarrhea, vomiting or gastric hemorrhage as the first symptom. The frequency of the various initial gastrointestinal complaints is summarized in Table II.

Roentgen studies of the gastrointestinal tract were carried out in 33 patients, or 63

TABLE I

SITE OF INITIAL SUPERFICIAL NODES IN 52 CASES OF HODGKIN'S DISEASE WITH GASTROINTESTINAL MANIFESTATIONS

Left neck	14
Left lower neck	11
Right neck	12
Axilla	4
Left submaxillary region	1
Suprasternal notch	1
Inguinal region	2
Unknown	2
No initial nodes	5

per cent of the cases. Of this group approximately 50 per cent failed to reveal any abnormality. The positive roentgen findings are given in Table III.

The average interval from the onset of the disease to the appearance of the gastrointestinal symptoms was two years and two months. This length of time approximates the average life expectancy in this disease which, according to numerous authors, is about two years and eight months.

The patients who developed gastrointestinal symptoms had an average life expectancy of three years and ten months, or one year and two months greater than the average life expectancy for all cases of Hodgkin's disease. Minot and Isaacs, in their analysis of a large group of lymphomas, also concluded that the duration of life was longer in those with symptoms referable to the gastrointestinal tract. On the other hand, we found that if the onset of the disease was with gastrointestinal manifestations then the life expectancy was short. The average duration of life in 6 pa-

TABLE II

INITIAL ABDOMINAL SYMPTOMS IN 52 CASES OF HODGKIN'S DISEASE WITH ABDOMINAL MANIFESTATIONS

Abdominal pain	19
Epigastric distress	16
Nausea and vomiting	5
Diarrhea	5
Dysphagia	3
Gastric hemorrhage	2
Flatulence	2

tients of this category was nine and a half months.

The explanation for the first phenomenon is probably that the patients who live longer develop the gastrointestinal complications. It is thought by some students of the subject (Symmers,¹³ Ewing,⁴ Desjardins³) that the retroperitoneal lymph nodes are involved early in the disease but fail to produce symptoms because, as they increase slowly in size, the abdominal organs are able to adjust to this growth for a long period of time. It is only when the viscera can no longer accommodate themselves to the enlargement of the masses that pres-

TABLE III

POSITIVE ROENTGEN FINDINGS IN 14 CASES WITH ABDOMINAL LYMPHOGNULOMATOSIS

Displacement of stomach or duodenum due to extragastric mass	2
Ulcer at the cardia	1
Deformity of lesser curvature	2
Irregularity of prepyloric region	1
Crater of the duodenal bulb (ulcer history)	2
Irregularity of duodenum	4
Pyloric defect	1
Narrowing of descending colon	1

sure symptoms arise. Hence these symptoms are a late manifestation and only those patients who live long enough develop them. The superficial, especially the cervical lymphadenopathy is but an external manifestation of this involvement. The finding that 37 out of 52 cases (71 per cent) in the present series had the original nodes in the neck tends to support this view.

A case that illustrates the relationship between cervical and retroperitoneal disease is the following:

The patient, a male, aged fifty-six, came to the clinic with the complaint of a hard swelling in the right side of the neck of three months' duration. Examination revealed several firm nodes on the right side of the neck, one of which was biopsied and reported as Hodgkin's disease. There were no other evidences of disease and a roentgenogram of the chest was negative. On the basis of these findings the case was thought suitable for surgery so a radical neck dissection

was performed, followed by deep roentgen therapy to the area. Within a year the patient developed epigastric distress, an abdominal mass and right supraclavicular and axillary nodes. A gastrointestinal examination showed displacement of the stomach probably due to upper abdominal disease. The patient succumbed less than one year later.

In those cases in which the initial symptom is referable to the gastrointestinal tract and the duration of life thereafter is short, intra-abdominal disease has probably been present for a considerable period although the patient may have been relatively asymptomatic and may have had no discernible external lymph node involvement. He may have had vague abdominal pains or aches, especially backache, for months without its significance being appreciated. When the gastrointestinal symptoms ultimately appear the patient is already in the terminal stage of the disease.

That Hodgkin's disease may be confined to the abdomen for a long period of time without external manifestations is illustrated by the following case:

The patient was a female, aged twenty-nine, whose initial symptom was weakness following the birth of her second baby. She developed a secondary anemia and progressive weakness over a period of eighteen months. Then she developed a lumbar backache and shortly thereafter a tumor was found in the left upper quadrant of the abdomen. There was no external lymphadenopathy. An abdominal exploration was performed at which a large retroperitoneal mass was found above the lesser curvature of the stomach. In the gastrohepatic omentum there was a mass of nodes which involved the stomach and there were numerous enlarged nodes along the greater curvature. One of these was removed and reported as cellular Hodgkin's disease.

The mass completely disappeared following high voltage roentgen irradiation and the patient was asymptomatic for four years. There was at no time any demonstrable superficial lymphadenopathy. One year later, or five years after the onset of the illness, a mass began to develop in the epigastrium associated with nausea and vomiting. Despite irradiation the condition grew worse until there was complete

pyloric obstruction. A gastroenterostomy was performed. The pyloric end of the stomach was involved in a mass which completely surrounded it. No enlarged nodes were found either in the gastrocolic or gastrohepatic omentum. She died three months later.

Enlargement of the retroperitoneal nodes may be accompanied by pyrexia. For this reason a diagnosis of appendicitis is occasionally made when the pressure produces right lower quadrant pain associated with fever. There were 3 such patients in this series. Two were subjected to laparotomy before coming to this clinic and the third refused operation despite the fact that his physician made a diagnosis of ruptured appendix with peritonitis.

Jaundice may occur in this disease due to pressure on the extrahepatic ducts by enlarged nodes or to pressure on the intralobular ducts by intrinsic liver disease. There were 4 jaundiced patients in this series.

Therapy is dependent upon the group in which the disease falls. In primary lymphogranulomatosis of the gastrointestinal tract the procedure of choice is surgery, even though the regional nodes may be involved. These gastric cases are usually explored because of a diagnosis of carcinoma. Gastros- copy should afford a means of making the correct preoperative diagnosis in some of these individuals. Gall⁵ has recently published statistics which show that cases of lymphoma which can be treated surgically have twice the life expectancy of those treated by other methods.

With secondary involvement and with extrinsic gastrointestinal disease the treatment is symptomatic. In addition to transfusion and general supportive measures the chief therapeutic agent is roentgen radiation. The superficial nodes as well as mediastinal masses are irradiated as they appear. The abdomen is irradiated for pain, epigastric distress, nausea, vomiting or diarrhea with excellent palliation. Attacks of pyrexia are also controlled by irradiating the retroperitoneal lymph nodes even though they may not be palpable. Many

patients are relieved of their symptoms for a longer or shorter period of time. This form of therapy does not increase the life expectancy but it does keep the patient comfortable and allows him to carry on for many months or several years in some instances.

SUMMARY AND CONCLUSIONS

1. There were symptoms referable to the gastrointestinal tract in 13 per cent of 406 cases of Hodgkin's disease studied at the Memorial Hospital from 1932 to 1942.

2. These symptoms may be produced by primary, secondary or extrinsic disease of the gastrointestinal tract.

3. Primary Hodgkin's disease of the gastrointestinal tract is a distinct entity whose treatment is surgical.

4. Secondary involvement of the gastrointestinal tract may be asymptomatic and discovered only at autopsy.

5. Gastrointestinal manifestations from secondary involvement or extrinsic Hodgkin's disease are usually a late occurrence and are found most frequently in the long lived patients.

6. If gastrointestinal symptoms appear early in the course of a generalized Hodgkin's disease the life expectancy as a rule is exceedingly short.

7. The clinical picture in some instances may resemble that of appendicitis.

8. Roentgen therapy may give considerable symptomatic relief in the cases of secondary or extrinsic Hodgkin's disease of the gastrointestinal tract but there is no evidence that the life expectancy is increased.

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PRIMARY MESOTHELIOMA (ENDOTHELIOMA) OF THE PLEURA

CASE REPORT

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WITHIN the past few years considerable literature has appeared on the subject of primary mesothelioma of the pleura. The varied nomenclature reflects the complexity of classifying primary diffuse pleural tumors. According to one group of writers,¹⁵ nearly two hundred authors have discussed and offered opinions on this entity describing the perplexities of the clinical, roentgenographic and pathologic phases. The clinicians and roentgenologists indeed have a difficult diagnostic problem when the pathologists, with a section of tissue under the microscope, argue among themselves as to type and histologic origin of the neoplasm.

Reviewing numerous statistics and data, Saccone and Coblenz¹⁵ concluded that the average frequency of this malignancy in necropsies is approximately 1.1 cases per thousand. The age distribution showed the greatest prevalence in the forty to sixty year bracket. Birnbaum³ stated that a predominance of the tumor in males existed in a ratio of about 2 to 1. There seems to be little difference in predilection of the pleural cancer for either right or left side of the thorax.

The clinical findings are quite variable and confusing, simulating the effects of a chronic inflammatory process and thereby masking the true malignant factor. Certain symptoms, nevertheless, predominate and are outstanding. Pain is persistent and appears early in the onset of the disease. A dry, irritating, non-productive cough soon appears. Hemoptysis is the unusual rather than the usual occurrence. Some dyspnea may be present and occasionally a low grade fever may exist. A rapid loss in energy and some loss in weight usually causes the patient to seek medical atten-

tion. Frequent respiratory affections are one of the major complaints of the patient.

Roentgen examination provides only little help in the early stages of the disease in attempting to identify the entity. A slight pleural effusion may be seen at the base of the involved lung. Later, the effusion becomes massive with obscuration of the entire lung field. Occasionally, tumor nodules can be demonstrated as in this case, but as a rule they are difficult to visualize. Doub and Jones⁴ advocate instillation of air following aspiration of the fluid in order to outline the tumor nodules and they state that "in few conditions is it of more value." A roentgen kymographic study may be of aid in differentiating a cardiac tumor from a pleural one, if the latter is in close relation to the cardiac silhouette.

Significantly, in performing a thoracentesis for the pleural effusion, the needle seems to strike a solid resistant tissue with difficulty in forcing the needle through the thickened pleura. This fact has been emphasized by several authors^{3,5,10,15} as a diagnostic aid. The pleural exudate may vary from a straw color, thin serous transudate to one of a hemorrhagic nature. Malignant cells may sometimes be found in the aspirated fluid but this finding is not pathognomonic of primary pleural cancer. DuBray and Rosson⁵ state that "cytodiagnosis is of limited value in the clinical diagnosis of malignant pleural disease." Saccone and Coblenz¹⁵ mention that a rapid reaccumulation of fluid occurs usually in a week or less following aspiration.

At necropsy, the macroscopic pathology presented is almost characteristic for this neoplasm. The pleura is irregularly thickened with firm, whitish, fibrous nodules

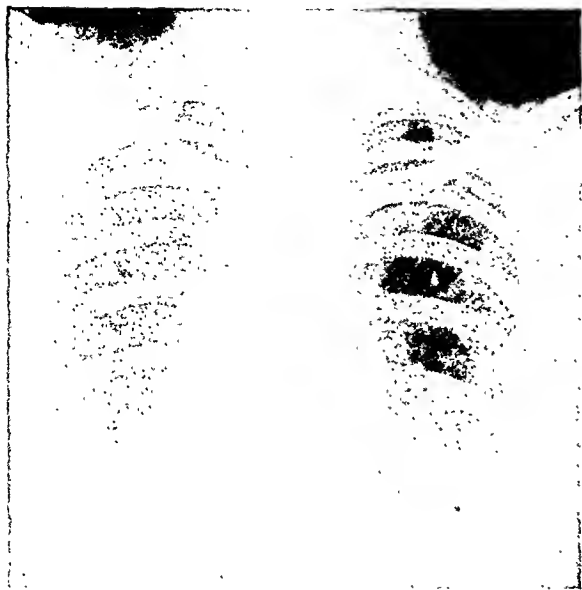


FIG. 1. The serofibrinous pleurisy at the left base of the lung can be visualized. No fracture of the ribs was discerned.

observed on the surface. The nodulations are conglomerate and diffuse, tending to encapsulate the lung and partially compress the lung parenchyma. Adhesions may fuse the layers of the pleura with often adherence of the pericardial sac to the malignant infiltration. Metastases are not common to distant organs, although cases have been reported with involvement in the kidney, spleen, adrenals, thyroid and brain. Metastatic bone invasion sometimes occurs in the ribs, and in our case the pelvis contained an extensive tumorous infiltration. There is wide extension in the majority of cases to all the surrounding areas and to the regional lymph nodes.

The microscopic picture reveals a prevalence of a fibrous stroma and the desmoplastic factor has been strongly emphasized by most writers. The tumor cells are of medium size, usually polyhedral, cuboidal or flat, and typically epithelial in appearance. These may appear as small alveoli, tubules, columns or nests. The nuclei are large, anaplastic and vesicular and very hyperchromatic, often showing pyknosis. Nucleoli are present in the cells and are usually faint. Lymphocytic infiltration may be seen in the pleural structure with evidence of chronic inflammation.

It is generally agreed that the pleura is derived embryologically from the mesoderm. However, controversy over the issue of the origin of pleural mesothelioma has resulted in several different views. The theory that the tumor arises from the endothelial lining of the pleura exclusively has the most support and adherents.^{12,15,18} Ewing⁶ and others^{1,8} advance the view that the pleural endothelium or the endothelial cells of the lymphatic vessels of the subpleural space are the site of origin for the new growth. Another theory^{9,11} strongly supported for a number of years was that the neoplasm originated only from the lymphatic endothelium of the pleura. Still others^{14,19} express the opinion that there is no such thing as a primary pleural cancer and that it is secondary to malignancy elsewhere, such as primary bronchogenic carcinoma. One group^{7,16} favors a hypothetical origin from aberrant nests of lung epithelium.

CASE REPORT

J.H.S., white female, aged thirty-three, in November, 1937, first visited a physician



FIG. 2. The cardiac silhouette is increased as compared with the examination fifteen months previously. The pleural exudate has become quite prominent with obscuration of the left costophrenic angle, and the left diaphragm is elevated and partially fixed. (An artefact can be seen in the right upper lung field.)

(Dr. F.L.U.) with the complaint of constant pain in her left lower anterior thorax. A dry, unproductive cough was present and the patient stated that intermittently she had a low grade fever. She related that she suffered a fall in 1936, striking her left thorax with her elbow. From that time on she noticed some pain on moderate respiratory effort. Shortly after the accident, she had an attack of influenza and was confined to bed for ten days. She resumed work as a dictaphone operator but soon gave up her job as a result of continual tiredness and loss of energy. The patient thought that she had a persistent fractured rib due to the accident.

Her past history was essentially negative except for an appendectomy and salpingectomy many years ago, and the removal of her tonsils. She had had the usual childhood diseases.

Physical examination revealed a rather well nourished white female in her early thirties, not appearing acutely ill, weighing 149 pounds. Temperature was 99.2°F., with a normal pulse and respiration. Head and neck were essentially negative, except for moderate dental caries. No



FIG. 3. A vertical fracture of the eighth left rib anteriorly is seen and appears of recent occurrence.

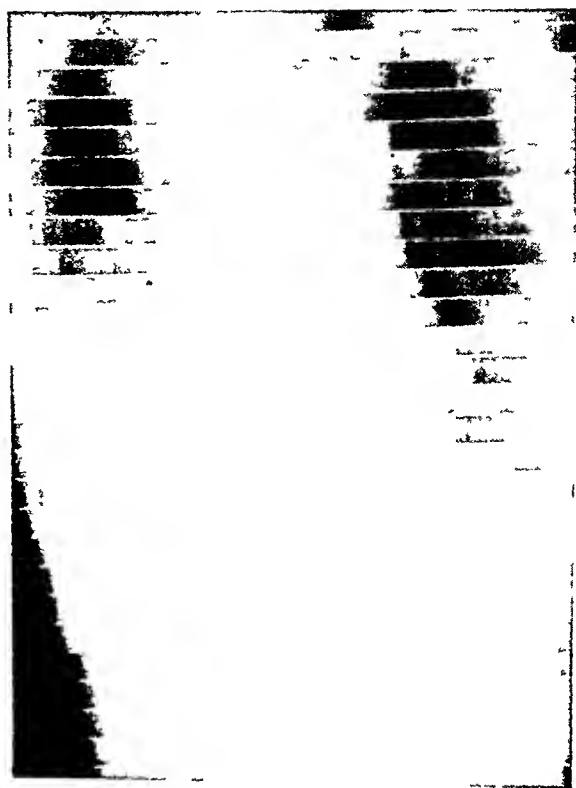


FIG. 4. A non-pulsating dense mass is noted in close relation to the left heart posteriorly and appears contiguous with the heart. Left oblique position.

tonsils were present. Auscultation of the heart disclosed no abnormality with no enlargement on percussion. Blood pressure 122/78. Localized tenderness over the eighth left rib anteriorly in the axillary line was found; however, no crepitus was obtained. The breast sounds were of the bronchovesicular type with no râles audible in either lung field. The abdomen showed a midline scar below the umbilicus; there were no palpable masses.

A roentgenogram was made of the thorax on November 9, 1937, with the following report: "The cardiac shadow appeared normal in size and shape. The left diaphragm was flattened with what appears to be a serofibrinous pleurisy over the left diaphragm. A limitation of motion and excursion of the left diaphragm could be seen fluoroscopically. No evidence of a fractured rib could be ascertained." The left thorax was strapped for a week. After this, the patient was not seen again for fifteen months.

The patient was next seen on February 6, 1939, by the same physician (Dr. F.L.U.), complaining of the severe constant pain in her left chest of varying intensity with soreness now in

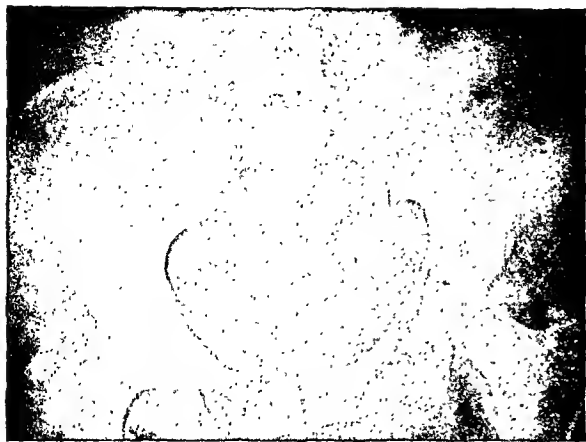


FIG. 5. Multiple osteolytic areas are observed in the bones of the pelvis after the administration of pitressin.

the small of her back. Dyspnea was quite pronounced on slight exertion and her husband remarked that when she slept a rather loud gurgling noise was evidenced during the respiratory phase. Loss in weight and protracted tiredness now were outstanding symptoms, as well as the dry cough.

Examination now showed a female with an early cachexia prevailing, weight 133 pounds. Temperature 99.4°F ., pulse 92 and respiratory rate 22. Positive findings consisted of marked flatness over the left lower thorax posteriorly with subcrepitant râles on auscultation at the left base. Breath sounds in the left lung were bronchial in character. Respiratory motion on the left was limited. Tenderness was again localized over the eighth rib on the left side in the anterior axillary line. Auscultation of the heart revealed the muscular and valvular sounds to be within normal limits except for a tachycardia. Blood pressure 126/74. The remainder of the physical findings were normal. Laboratory findings were not unusual and were within the normal limits.

A roentgen examination of the chest was made on February 14, 1939. The following findings were reported: "Vertical fracture of the eighth rib on the left side somewhat anteriorly. The cardiac silhouette is considerably enlarged both to the right and left as compared with the previous exposure taken fifteen months ago, with a straightening of the left heart border. There is an obscuration of the left lower lung field as the result of pleural exudate with an eventration of the left diaphragm as evidenced under fluoroscopy. Considerable

hilar and central root branch thickening is observed on both sides extending towards the bases. Thickening of the right upper interlobar septum was noted."

In view of the roentgenographic findings, the patient was referred to a cardiologist (Dr. R.C.P.) for consultation. His findings were essentially negative except for a sino-auricular tachycardia evidenced on the electrocardiogram. The increase in the cardiac dimensions were confirmed, as well as the pleural effusion at the left base. Palliative therapy was given for the pain in the way of mild analgesic medication and the patient was requested to return in a few weeks for another roentgen examination of the chest.

On March 31, 1939, a roentgen kymogram of the chest was made with the following findings: "The marked cardiac enlargement is as previously reported, more marked on the left. What appears to be a pleural exudate is observed at the left base behind the cardiac shadow and extending slightly up the lateral thoracic wall apparently due to capillary attraction. A dense mass about the size of a small egg is seen roentgenoscopically and kymographically in the left oblique position arising from the region of the lower left heart silhouette and in close relation to the cardiac shadow with a shifting of positions. There did not appear to be any definite pulsation of the tumefaction apparently

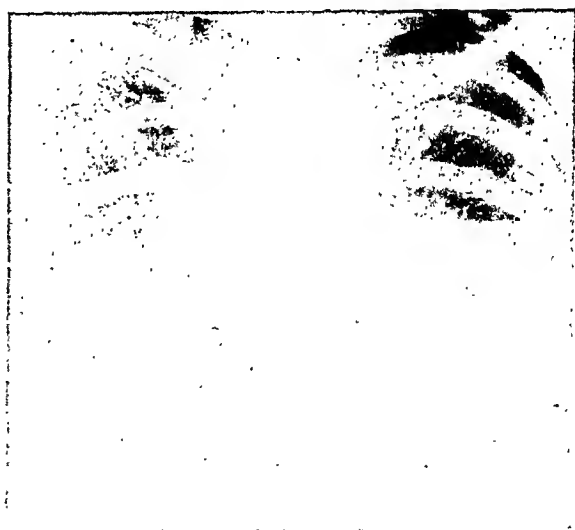


FIG. 6. The pleural effusion, fluid level and partial left pneumothorax are quite evident. The metastatic nodules in the right lung are of diffuse distribution.

arising from the left ventricle or pericardium at this site." A tentative diagnosis of a bronchogenic cancer was made with several other possibilities suggested, such as a rare cardiac neoplasm. Pleural mesothelioma was mentioned as a remote possibility.

Shortly after this the patient began to complain of pain in the pelvic region and lumbosacral spine. The pelvis was roentgenographed on May 5, 1939, following the administration of 1 cc. of pitressin intramuscularly, and the following findings were noted: "Several zones of radioparency in the region of the right iliac crest at the outer margin and near the left anterior inferior iliac spine could be discerned, as well as in the area of the right sacroiliac synchondrosis. The entire picture presents one of metastatic infiltration from a malignant growth." It was then felt that we were dealing with a primary pulmonary carcinoma secondarily involving the pericardium and pleura, with metastases to the rib and pelvis.

Palliative radiation therapy was administered to the thorax and pelvis for the agonizing constant pain. The factors were: 200 kv. constant potential; filtration 0.5 mm. copper plus 1.0 mm. aluminum in addition to the inherent filtration of 0.25 mm. copper; target-skin distance 50 cm.; 15 ma.; half-value layer 1.1 mm. copper. The pulmonary fields were confined to the left thorax and were three in number. The anterior and posterior fields were 15 by 15 cm. and the lateral field was 10 by 10 cm. The dosage was 200 roentgens (measured on the



FIG. 7. Photomicrograph of left pleura ($\times 80$). Hematoxylin-eosin stain. Note the plexiform cords of tumor cells. The neoplastic cells can be seen lying in the lymph spaces as well as lining the lymph channels.



FIG. 8. Photograph of gross specimen of heart and lungs. The heart can be seen in the center of the specimen with the right lung uncompressed, and tumor nodules can be noted at the base. The left lung is markedly compressed and atelectatic, and is situated towards the rear of the specimen.

skin) given daily to one of the three fields, alternating the fields so that each one was treated every fourth day. The total dose delivered to each field was 2,000 r. Four pelvic fields were used, each 15 by 15 cm. (left and right anterior and posterior). A daily dose of 200 r was given to one field until a total dose of 1,000 r was administered to each of the four fields. Slight relief from the intense pain in the pelvis was observed after several treatments, but this was transient. A complete blood count was made near the termination of the course of irradiation, with the blood picture found to be within normal limits.

Shortly after irradiation was begun thoracentesis was performed to increase the effect of the roentgen therapy. The first was done on May 15, 1939, and 1,000 cc. of clear straw-colored fluid was aspirated. Some difficulty was noted in forcing the aspirating needle into the pleural space. This was casually mentioned and failed to impress us as a diagnostic feature. Aspiration was continued about every two weeks for four occasions and the exudate was serous and of a clear, amber color. Thoracentesis was always difficult to accomplish. No malignant cells were found microscopically in the aspirated fluid.

Roentgen therapy was limited due to acute respiratory embarrassment. A roentgenogram of the chest was taken soon after the completion of the roentgen treatments, on July 7, 1939. "A pleural effusion in the left lung with a fluid

level was discerned. A left partial pneumothorax is also noted. The right lung shows a diffuse mottled infiltration throughout and is probably metastatic invasion from the primary neoplasm. The enlargement of the cardiac silhouette is primarily to the left and may be due to pericardial sac retraction or effusion."

Later, the patient decided to go to Louisiana to visit her family. She remained there for approximately two months and while there was "tapped" twice and also given neoprontosil by mouth. She returned the first part of September, 1939, for observation and further care. Aspiration was again performed on September 10, 1939, and the fluid obtained was clear, bright red but did not have the viscosity of blood. Two more aspirations at ten day intervals were done, frank blood being obtained each time.

Dyspnea became quite pronounced and death ensued, typical of respiratory failure, on October 5, 1939. Just before death, she complained of severe pain of marked intensity in the pelvic region.

Autopsy. This was performed by Dr. Leo Lowbeer of Hillcrest Memorial Hospital, Tulsa, Oklahoma, on October 5, 1939. *Gross macroscopic examination* revealed a highly emaciated and anemic white woman with no evidence of cyanosis, edema or jaundice. The chest contained approximately 2,000 cc. of serous amber fluid in the right pleural cavity with no pleural adhesions noted. The right parietal and visceral pleurae were not thickened, although small tumor nodules were scattered throughout the entire surface of the pulmonary component. The left visceral pleura was firmly adherent to the pericardium on one side and to the parietal pleura of the upper lobe on the other side. An encapsulated exudate of about 1,000 cc. of rather cloudy, bloody fluid was found between the thickened layers of the visceral and parietal pleurae of the lower lobe. Almost the entire left visceral and parietal pleurae were altered, having a whitish appearance and being greatly thickened with adherence of the layers of the pleurae to each other as in the upper portion of the thorax, or forming pockets or sacs containing masses of fibrin, blood clots or serous fluid as in the lower thorax. The contiguous surfaces of the thickened pleurae presented numerous small whitish nodules. The entire left lung, especially the lower lobe, was small, compressed and atelectatic. On cut section, several small

white nodules were found in the lung. The right lung showed some compression with numerous nodules scattered in both the upper and lower lobes. The large and small bronchi did not reveal any tumor arising from the mucosae of the bronchi. The mediastinal lymph nodes were infiltrated by the firm whitish tumor metastases.

The pericardial cavity was distended and also filled with fluid. The inner surface of the pericardial sac was covered with whitish gray neoplastic nodulations apparently penetrating from the adherent left visceral pleura. The heart was not enlarged, and did not show any pathologic change. The valves were normal and unaltered.

The eighth left rib was the seat of a cherry-sized osteoclastic metastasis.

Both breasts were normal, with no malignant infiltration.

An old incision in the midline of the lower abdomen was noted. Permission was not granted for examination of the abdominal contents; however, the abdominal cavity was inspected through the thoracic incision. The liver, spleen, kidneys, peritoneum and pelvic organs revealed no evidence of involvement by the neoplasm. Adhesions were observed in the pelvis with an absence of both uterine salpinges.

Microscopic examination revealed the left pleura to be enormously thickened, consisting of a fibrous stroma containing numerous, often densely packed alveoli, tubules, columns, nests and sheets of tumor cells. The cells were polyhedral or cuboidal in appearance, resembling epithelial cells with large anaplastic, pleomorphic, mostly round, very hyperchromatic, or even pyknotic nuclei. Solid nests and columns of these malignant cells could be seen filling and distending the countless lymph spaces all over the pleura. In some areas, an alveolar arrangement of the neoplastic cells occurred, while in others they seemed to line the lymph vessels. Occasionally, a solid plexiform structure of cells was observed with pearl-like formations resembling squamous cell carcinoma. The formation of lumina was discerned in some of the solid nests of tumor cells. Mitotic figures and some tumor giant cells were noted. The pleura showed evidence of chronic inflammation with lymphocytic infiltration. On the visceral surface, the pleura was covered with a thick layer of fibrin. The diaphragm did not reveal any tumor invasion.

The histopathological structure of the lung

metastases resembled that described in the primary pleural tumor, with the malignant cells frequently replacing the alveolar epithelium and lining the lung alveoli. The lumina of these alveolar structures often remained or were filled by masses of tumor cells.

The mediastinal lymph nodes contained metastatic cells forming solid alveoli and bands embedded in old hyaline fibrous scar tissue enclosing considerable anthracotic pigment. The cells were often arranged to form a lumen with the cells flattened in single rows simulating lymph spaces.

Pathologic Diagnosis: (1) primary mesothelioma (endothelioma) of the left pleura with an old encapsulated pleural serofibrinous-hemorrhagic exudate; (2) complete compression atelectasis of the left lung; (3) metastases to the pericardium with serofibrinous pericarditis; (4) metastases to the right visceral pleura with serofibrinous pleurisy; (5) metastases to both lungs especially the right; (6) metastases to the mediastinal lymph nodes; (7) osteoclastic metastases in the eighth left rib and pelvis.

COMMENT

The relative infrequency of this tumor, as well as the confusing clinical and roentgenologic features, has led us to submit a report of this case. The early symptom of constant pain with loss in energy, plus the persistent pleural effusion and difficulty in aspiration, should have made us strongly suspect the presence of a malignant pleural neoplasm in view of the roentgenographic findings. The increasing diameter of the cardiac silhouette to the left suggested a heart disease in spite of the lack of other cardiac confirmatory evidence and confused the diagnosis. The roentgen kymographic study indicated a non-pulsating tumor but the contiguity with the heart shadow made it appear that we might be dealing with a rare cardiac neoplasm. It is interesting to note the duration of the symptoms. For over a period of two years the patient had the intense gnawing pain in her left lower thorax, interpreting it as the result of an injury sustained to this region. Undoubtedly the rib invasion was in close conjunction with the onset of the

disease. The rib fracture had the appearance of a recent one, with no roentgen signs of a metastatic process, either osteoclastic or osteoplastic. The history of a single acute trauma again brings up the much discussed point as to what part trauma¹³ did play in the disease. It is believed that the blow to the thorax was coincidental, although it is quite possible that it may have prepared the site for the metastasis by lowering rib resistance (localized hemorrhage and interference with circulation).

The question arises as to what effect radiation therapy has on this type of neoplasm. The mere presence of anaplastic cells together with their debatable histologic origin alone does not indicate that this new growth is radiosensitive in that the desmoplastic matrix of the mesothelial cellular elements would tend to negate these factors. Little definite irradiation effect could be ascertained in the microscopic findings. To a slight degree, the hyperchromatism, pyknosis, lymphocytic infiltration and fibrous connective tissue stroma may have resulted from irradiation but this is to be questioned in that the same changes have been described by various authors^{12,15} in untreated cases. Possibly dosage was inadequate since the therapy was terminated on the thorax after a total of 6,000 r on the skin because of the patient's respiratory discomfort. A tumor dose could not be determined with any degree of accuracy on account of the persistent pleural effusion and the diffuseness of the lesion. The obstructive phenomena in the lymph channels by tumor cells observed microscopically may have interfered with the cell-fluid exchange increasing the effusion in the left chest cavity. Stewart and Farrow¹⁷ mention that one case of pleural endothelioma, treated by radiation therapy, showed no response after a dosage of 6,000 r. Others^{10,18} have mentioned the use of roentgen therapy as a palliative measure with temporary improvement clinically. The doses have varied from 5,000 to 6,000 r, with no reference as to whether these were tumor or

skin doses. Microscopic alteration or influence on the tumor following irradiation has not been previously alluded to and it is to be wondered to what extent irradiation influenced the neoplasm to bring about improvement, if any.

The next question is whether or not irradiation increased the atelectatic and fibrosing processes in the left lung. Only speculation can be made in an attempt to answer this question. If the mesothelial cells were not affected, then one could hardly expect the fibrous connective tissue to be influenced, and stroma of this type could occur only as the end-result of intense irradiation. Nevertheless, it must be kept in mind that a stimulating dose might have been given the neoplasm. The value of roentgen therapy in this condition is difficult to determine, and more histopathologic studies should be made in order to properly interpret its efficacy.

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The author wishes to thank Dr. F. L. Underwood and Dr. Leo Lowbeer, of Tulsa, Oklahoma, for their cooperation and permission to report this case.

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UNUSUAL URINARY CALCULI

BRIEF REVIEW OF THE LITERATURE AND REPORT OF SIX CASES*

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IN JULY, 1896, only six months after Röntgen discovered the x-ray, James Adams, a Glasgow Surgeon, first detected roentgenographically and successfully removed a renal calculus. Usually, one can recognize a calculus from the plain roentgenogram, but in many cases excretory or retrograde pyelography or both are necessary for exact diagnosis and localization.

This discussion will be limited to a few of the more interesting recorded cases and a report of our 6 unusual cases of urinary calculi selected from patients studied at the Misericordia Hospital during the past seventeen years. The diagnosis of these cases could be easily made from the plain roentgenogram alone; and the calculi are of unusual interest because of their size, location and history of development.

Since the introduction of intravenous urography by von Lichtenberg and Swick⁴³ in 1929 the literature on urinary tract disease has greatly increased, and it has been estimated that about 80 per cent of urinary tract studies have been made for the determination of the presence or absence of urinary calculi.

REVIEW OF THE LITERATURE

Caulk⁷ reported giant coral stones which completely filled the pelvis and calices of both kidneys. The right calculus measured 12 cm. and the left 16.5 cm. in their vertical diameters. There was also a bladder stone 8.5 cm. in diameter.

Harries,¹⁹ in 1937 described a case of bilateral renal calculi in a male, aged fifty-two, in which the right kidney stone weighed 24 ounces and the left 9 ounces. The chief complaint was a lump in the right side which appeared nine months previous to his admission to the hospital.

Cecil⁸ reported a hollow right renal stone 3.5 by 3 by 2 cm. in a male, aged thirty-one. The patient was kicked by a horse at the age of three, and the lower right ribs were fractured.

Stevens³³ reported a case of bilateral giant ureteral

calculi in a male, aged thirty-three. The left weighed 50 grams, the right 18 grams.

Randall³⁵ described the largest bladder stone on record; it measured 48 cm. in its greatest circumference and weighed 64 ounces wet and 56 ounces when dry.

Holman²⁴ reported a urethral stone in an eight and one-half months pregnant woman. Several months before, she attempted abortion with slippery elm. A piece of elm bark was found as the nucleus. The stone measured 2½ by 1½ inches in diameter.

In 1943, Higgins²² of the Cleveland Clinic reported 7 cases of urethral stones in a twenty-two year period after 1921.

Graham¹⁸ described the case of a male, aged fifty-two, with pain and swelling in the perineum. In 1930, the patient was kicked between the legs. For the next two weeks he had occasional hematuria; later a perineal abscess developed which left a draining sinus. In 1938 he developed acute retention and a lump the size of a hen's egg, in the perineum. The removed calculus from the posterior urethra weighed 24 grams.

LeComte²⁹ noted that calculi seldom lodge in the male urethra. He found only 7 instances in 2,900 urological cases. He also mentions a case in which 230 stones were passed.

Brooksher⁵ reports the case of a male, aged forty, who, two years before study, had a series of right renal colic and passed four stones one year later. He was symptom free for one year, then he had difficulty in voiding. By manipulation with the scope a stone was passed from the urethra.

Englisch¹⁵ observed that about 42 per cent of urethral calculi are in the membranous portion and 48 per cent in the anterior portion of the urethra.

Joly²⁶ noted that 18 per cent of urethral calculi are associated with calculi elsewhere in the urinary tract.

Up to 1943, Lane²⁸ found 39 cases of urethral calculi in the literature and added 1 of his own.

Debenham⁹ recorded 40 cases of urethral calculi admitted to the London Hospital over a twenty year period, from 1910 to 1930, thirty-seven of which were impacted or secondary calculi and only 3 were primary urethral calculi. Thirty-four of 37 cases of secondary calculi were in males and only 3 in females. The 3 primary cases were all associated with urethral stricture of long standing.

Seymour³⁷ reports the case of a male, aged seventy-one, with a diverticulum of the urethra the size of a hen's egg filled with many stones.

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FIG. 1. Case 1. Intravenous urogram showing a large fragmented dendritic calculus completely filling the structures of the right kidney; no excretion from this kidney. The left kidney functions normally.

Heckel and Johannesen²⁰ report the case of a male, aged sixty-three, with a primary urethral calculus the size of an olive.

d'Offay¹¹ published the case of a male, aged sixty-six, who nineteen years before, had injured his perineum. He suffered considerable pain following the injury but sought no treatment. Three years later he developed difficulty in passing his water. The stream became very thin one year before admission. He felt a lump in the perineum. The removed stone measured $\frac{7}{8}$ by $2\frac{1}{4}$ inches.

Thomson¹⁰ reports the case of a male, aged fifty-five, who for ten years had passed gravel, with some pain and frequency. The removed urethral stone measured $2\frac{1}{2}$ by $1\frac{1}{2}$ inches. The majority of urethral calculi are associated with local dilatation or diverticulum secondary to chronic obstruction. The generally accepted predisposing cause for all urinary calculi are obstruction, stasis and infection. Many of the reported cases do not specify whether ureteral or urethral stones are primary or secondary. The great majority of these calculi are, however, secondary. We have seen several calculi develop in the site from which a stone had been previously removed undoubtedly due to trauma and associated stasis and obstruction.

CASE REPORTS*

CASE 1. A male, aged sixty-three, was admitted to the Misericordia Hospital, June 17,

* We are indebted to Dr. A. E. Bothe, Genito-urinary Surgeon to the Misericordia Hospital, for permission to report 3 of these cases.

1943, because of gastric distress, loss of appetite, general weakness, dyspnea and edema of the ankles. In 1927 the patient had a stone removed from the right kidney. At present, sixteen years after the kidney operation, there is a hard mass easily palpated through the thin relaxed scar in the right kidney region which is especially prominent during coughing or straining, indicating a large incisional hernia. Nearly the entire kidney can be distinctly felt through the herniated relaxed scar. The presence of a large calculus in this kidney was suggested by the surgeon even before the roentgen examination was made. The general condition of the patient was obviously poor. There were no complaints of the patient in regard to the right kidney except that he mentions a lump and big scar in the right kidney area.

Urinalysis: Sp. gr. 1.021, albumin 3 plus, loaded with pus cells, and calcium oxalate crystals.

Roentgen examination of the abdomen shows definite enlargement of the liver. The left kidney is moderately enlarged and unusually dense. The right kidney is apparently normal in size but contains a huge calculus completely filling the pelvis, calices and uppermost portion of the ureter, all of which structures are greatly enlarged. There is a complete fracture through the base of the upper part of the calculus at its junction with the pelvic portion.



FIG. 2. Case 1. Close-up roentgenogram of the large fragmented dendritic calculus.

The greatest vertical diameter of this dendritic calculus as measured from the roentgenogram is 12.5 cm.; its greatest transverse diameter 6.5 cm. Intravenous urography shows the appearance of the dye in the pelvis and calices of the left kidney five minutes after the injection. There is no dilatation, obstruction or any other abnormality in the left urinary tract. The bladder is well distended and is normal in contour except for pressure effect on its inferior margin suggesting enlarged prostate. The cortex of the right kidney seems to be reduced to a thin membrane only about 5 mm. in thickness. Six days after admission, a right nephrectomy was performed.

Pathological Report: The entire removed specimen weighed 240 gm. The specimen is completely filled with palpable stones. The calculi from the specimen weighed 100 gm. In the mid-pelvis there is a point of articulation with faceted surfaces. The calices are greatly dilated and contain granular debris. Microscopic section showed marked reduction in stroma and tubular elements. Diagnosis: Nephrolithiasis, pyonephritis. Patient died twenty-four hours after operation of cardiac failure.

CASE II. A female aged sixty-three, was admitted to the Misericordia Hospital, August 18, 1940, apparently in good health. About four weeks previous to admission, she sustained a slight back injury in Florida. The roentgen ex-



FIG. 3. Case II. Plain roentgenogram of the abdomen showing a large heart-shaped opacity in the upper pole of the right kidney.



FIG. 4. Case II. A close-up of the large calcified area which proved to be a healed tuberculous lesion, producing no symptoms.

amination at that time showed no evidence of fracture or other injury but she was told that she had a large stone in the right kidney and to see her doctor when she returned to Philadelphia. In 1905 at the age of twenty-eight, patient was pronounced "tubercular" and spent two years in a sanatorium. At the present time patient has only slight backache and is worried about the large right kidney stone. Blood and urine examinations were essentially negative.

Roentgen examination, on August 18, 1940, the day of admission shows on the plain abdominal roentgenogram a sharply defined calcified mass 6 by 5 cm. somewhat heart shaped, located either in or on the upper pole of the right kidney. This corresponds in shape and position with the suprarenal gland. Intravenous urography shows the appearance of the dye in the pelvis and calices of both kidneys five minutes after the injection. These structures are reasonably well filled and show nothing abnormal. The thirty-five minute urogram shows good drainage from both sides, no obstruction or any other abnormality. Oblique views show that the calcified body retains the same relation with the upper pole of the right kidney in all views. The possibility of an enlarged calcified adrenal gland is suggested. There were no clinical symptoms to support this possible diagnosis.

August 22, 1940, through a posterior incision,



FIG. 5. Case III. Plain roentgenogram of the abdomen showing the large calculus in the lower portion of the left ureter which developed several years following left nephrectomy. A calculus is also shown in the region from which the left kidney has been removed.

the right kidney was exposed; slightly less than the upper fourth of the right kidney was removed with possible incorporation of the right suprarenal gland. Patient made an uneventful recovery.

Clinical Diagnosis: Tuberculosis of the kidney. Gross description: Specimen consists of a cystic mass measuring 6 by 5 by 3.5 cm. The wall of the cyst is thick and fibrous; the lumen contains a large amount of white pasty opaque fluid. Microscopic examination: The gross findings and histopathologic pictures are consistent with a diagnosis of healed tuberculosis of the kidney. Patient made an uneventful recovery.

CASE III. Female, aged seventy-two, admitted to the Hospital August 22, 1944, because of nausea and vomiting; frequency of urination and burning pain in the bladder region. Temperature, pulse and respiration, normal. Urinalysis: sp. gr. 1.017, negative for albumin, pus cells and casts.

November 14, 1935, patient had a cystostomy for the removal of a vesical stone. April 15, 1936, had left nephrectomy for left renal stone. Patient was again admitted on April 26, 1938, for left retroperitoneal abscess which was

incised and drained. The wound continued to drain for many months. November, 1938, the sinus tract was injected with viscid skiodan. This showed a narrow sinus tract communicating with the area from which the kidney had been removed. The kidney bed is represented by an accumulation of the opaque material producing a shadow comparable in size and shape to a gall bladder. The entire left ureter is well outlined with the solution and is moderately dilated down to a point corresponding to the position of the left ureteral orifice. Not any of the skiodan entered the bladder. The sinus tract is therefore communicating with a patent left ureter which is dilated and apparently obstructed at the ureteral orifice. There is a calcified body in the left kidney region. The plain roentgenogram showed an additional laminated calculus about 0.5 cm. in diameter located about 2 inches above the left ureteral orifice.

The recent roentgen examination, August 23, 1944, shows on the plain roentgenogram two calcified bodies, one 1.25 cm., the other 0.5 cm. in diameter located in the left kidney area. There is a large calcified body located in the lower portion of the left ureter 7 cm. in length and slightly more than 1 cm. in its greatest transverse diameter, indicating a large left ureteral calculus.

This calculus has therefore developed from a

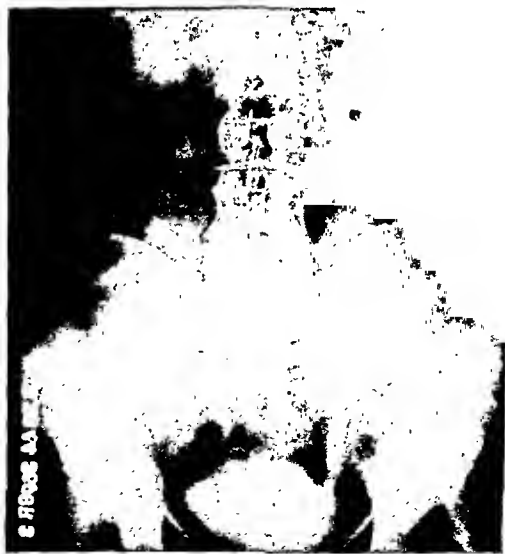


FIG. 6. Case III. Intravenous urogram showing good right kidney function as indicated by the amount of dye in the bladder, after about thirty minutes. The large calculus is again shown in the lower portion of the left ureter.

small stone which was present in 1938. At that time the calculus in the lower ureter measured about 0.5 cm. in its greatest diameter. This calculus has developed to its present size since the removal of the left kidney.

CASE IV. Male, aged thirty-seven, admitted June 7, 1936, because of pain and swelling in the lower abdomen and general weakness. For the past two years patient has had a sharp pain at frequent intervals in the left side lasting about one hour, gradually becoming more severe and more frequent. For the past two weeks, pain has been constant. Patient has chills, frequency and burning after urination. Past history: General health, fair. Has had four operations for recurring double inguinal hernia. At the age of eight, he fell astride a fire-plug injuring his penis and urethra. Has had sounds passed for urethral stricture since that time up to twelve years ago. On admission, temperature varies from 99 to 102° F.; pulse 80 to 120; respirations 24.

Roentgen examination at this time, twenty-nine years after injury, shows an indistinct outline of the right kidney which appears to be larger than normal. The left kidney outline is not clearly shown, but there seems to be a soft tissue mass in the left kidney area. There is a large calcified body 20 cm. long and 3.75 cm.



Fig. 7. Case iv. Intravenous urogram showing two of the dilated upper calices of the right kidney; no excretion from the left kidney up to one and one-half hours, and a huge articulating calculus in the lower left ureter.



Fig. 8. Case iv. A close-up of the calculus which is probably the largest recorded ureteral stone.

at its widest point, measured from the roentgenogram, located in the lower left quadrant divided by what appears to be an articulation below its middle, apparently located in the lower half of the left ureter. There is also an oval laminated shadow in the region of the lower pole of the right kidney, probably a right renal calculus. Intravenous urography shows the appearance of the dye in the calices of the right kidney ten minutes after the injection. The calices are markedly dilated. Here again the calculus is shown in the lower pole of the right kidney. None of the urograms show any of the dye in the structures on the left side up to one and one-half hours after the injection.

June 7, 1936, under ether anesthesia, a left inguinal incision was made. A large quantity of thick yellow pus was found in the region of the ureter and left kidney area. A rubber tube was inserted for drainage. No attempt was made at this time to remove the large ureteral stone.

July 6, 1936, a suprapubic incision was made to the left of the midline. The bladder was identified and the peritoneum reflected upward by dissection. The left ureter was isolated, incised and opened. The lower of the two calculi was removed, with some difficulty, in one piece. The upper stone was finally removed with great difficulty; this crumbled and was removed by stone forceps and syringe. The removal of the uppermost portion of the stone was followed by the flow of about 350 cc. of yellow thick pus down the left ureter. A large rubber tube was



FIG. 9. Case v. Large calculus in the prostatic portion of the urethra proved by operation.

inserted into the left ureter and connected to a drainage bottle. The prevesical space was packed with gauze and a cigarette drain.

The urine on admission showed from 1 to 2 plus albumin, sp. gr. 1.010 to 1.018, from few to many pus cells, amorphous and triple phosphates; red blood cells 4,500,000; leukocytes from 11,000 to 15,000. Blood chemistry: blood urea nitrogen, 22; blood sugar, 115.

August 12, 1936, nephrectomy was performed through a posterior incision. Pathological diagnosis: Chronic pyonephrosis, left kidney measuring 11 by 6 by 5 cm. Pelvis greatly dilated, calices obliterated.

Drainage was free for the following months and the patient pursued a slow but gradually retrogressive course and died on May 31, 1937.

CASE v. Male, aged twenty-nine, admitted to the Misericordia Hospital, November 7, 1927, with pain in the region of both kidneys of seven months' duration radiating to the scrotum, particularly on the right side. The pain was associated with frequency and burning. He has never noted any blood in the urine and denies venereal infection. He has had night sweats, cough and occasional hemoptysis. Urinalysis: sp. gr. 1.025, heavy trace of albumin, many leukocytes. No tubercle bacilli in sputum or urine. Wassermann test, negative. Temperature, pulse and respiration normal.

Roentgen examination of the chest showed irregular mottled infiltration in the apex of the right upper lobe with contraction of the thoracic cage in this area and lesser involvement

in the left apex. The appearance indicates bilateral chronic fibroid tuberculosis.

Roentgen examination of the abdomen and pelvis made November 10, 1927, shows a bullet-shaped calcified body located in the region of the neck of the bladder measuring 3.75 cm. in its longitudinal and 2 cm. in its transverse diameter, indicating a large calculus located probably in the vesical neck. A clinical diagnosis of posterior urethral calculus had been made by the urologist but the location of the concretion on the roentgenogram seemed to be somewhat above the usual position of the prostatic urethra.

Cystoscopic report, November 11, 1927: A grating sensation was felt as a large cystoscope was passed through the posterior urethra. No residue of urine. The bladder neck, mucous membrane and ureteral orifices appeared normal. Trigone is slightly congested. When the scope was withdrawn about one inch from the posterior urethra, a lobulated stone lodged in a diverticulum was seen. Rectal examination revealed the prostate stony hard and nodular. Diagnosis: Large calculus located in a diverticulum in the prostatic urethra.

November 18, 1927, under sacral anesthesia, the calculus was removed through a perineal incision. The prostate was identified, an open-



FIG. 10. Case vi. Two calculi in a diverticulum in the anterior urethra. There are also numerous small calculi in the prostate gland.

ing made into the posterior urethra and the calculus extracted. Patient discharged cured December 19, 1927.

CASE VI. Male, aged seventy, admitted to the Misericordia Hospital November 23, 1942, suffering from acute retention of urine. At the age of thirty-six (thirty-four years ago) the patient fell astride a wagon-wheel, rupturing his urethra which was repaired a few days later. No history of venereal disease. At intervals of a few months during the past thirty-four years patient has suffered from attacks of acute retention. At such times a warm bath would enable him to pass a catheter and thus obtain relief. Many sounds have been passed for dilatation of the urethral stricture with no apparent permanent benefit. Temperature, pulse and respiration normal. Urinalysis: sp. gr. 1.015, albumin plus 2; blood urea nitrogen 11.

Intravenous urography November 24, 1942, showed the appearance of the dye in the pelvis and calices of both kidneys five minutes after the injection. There was considerable output after only twenty minutes, indicating good renal function. The bladder wall is slightly thickened and suggests chronic cystitis.

A small roentgenogram made of the bladder area twenty minutes after the injection shows two sharply defined oval calcified bodies, one 1.5 cm., the other 0.5 cm., located in the midline approximately in the middle third of the anterior urethra. There are also a few small calcified bodies beneath the pubic arch suggesting prostatic calculi.

November 25, 1942, patient had acute retention; a catheter could not be passed and a suprapubic cystostomy was performed. A sound was passed through the bladder into the posterior urethra and another sound was passed into the anterior urethra. An incision was made over the sound in the posterior urethra through a dense fibrous stricture and two stones were removed. A suprapubic tube was placed in the bladder and a catheter passed through the penile urethra into the bladder. After four weeks a flexible bougie was passed and the patient was discharged in good condition December 24, 1942.

DISCUSSION

Six cases of unusual urinary tract calculi have been presented. Case 1 is of special interest because of the large size of the den-

dritic stone (12.5 by 6.5 cm., weighing 100 gm.); the long period for its development (sixteen years); the marked mobility of the kidney in a large incisional hernia; the recognition of the stone by palpation, and the presence of a fracture which proved to be an articulation.

Case II impressed us as being an odd picture of healed tuberculosis, because of the sharp definition and shape of the dense shadow in the upper pole of the left kidney. There was no disturbance of function or distortion of the pelvis or calices, but there is an old history (thirty-five years ago) of pulmonary tuberculosis. From the roentgen studies calcification of the left adrenal gland was suggested.

Case III is of unusual interest because of the large size of the ureteral concretion (7 by 1.25 cm.); its development for the most part during the six years following left nephrectomy.

Case IV we believe is the largest ureteral stone ever reported. It developed during a twenty-nine year period following an injury to the penis and urethra, several plastic operations and four herniorrhaphies for bilateral recurring inguinal hernias. It developed into two articulating fragments.

Cases V and VI. According to the literature primary calculi in the urethra are rare. In Case V, the large calculus developed in a diverticulum in the prostatic urethra and in Case VI, the two calculi developed in the anterior urethra, posterior to a urethral stricture. With one exception these cases illustrate that obstruction, stasis and infection are the predisposing causes of urinary calculi.

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MASSIVE CALCIFICATION OF THE LIVER*

CASE REPORT WITH A DISCUSSION OF ITS ETIOLOGY ON THE BASIS OF ALVEOLAR HYDATID DISEASE

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A CASE of massive calcification of the liver parenchyma has been encountered recently which is thought worthy of reporting together with a discussion of its probable etiology.

Calcification in many organs of the body is commonly seen on roentgenographic examination, but its occurrence within the liver parenchyma is not. Its occurrence in the liver upon roentgen examination of the abdomen and the etiological factors have been commented upon.⁴ In a series of 8,000 autopsies massive calcification of the liver parenchyma was observed only once and its etiology was undetermined.³

Echinococcus disease is probably the commonest cause of calcification within the liver and the unilocular variety is by far the most common and most widespread. The unilocular hydatid cyst if unrestricted in its growth is oval or round in shape.^{1,2,5} Its wall consists of two layers—an outer chitinous cuticle with characteristic laminations facing the protective fibrous capsule of the host and an inner germinal layer. The growth of the germinal layer by *invagination* produces daughter cysts which contain scolices. These, in turn, may form granddaughter cysts. Around the mother sac of this unilocular cyst a protective fibrous tissue capsule is developed from the tissues of the host. As the parasite grows older and larger, areas of degeneration may occur in the host's capsular tissues. Calcium deposits may be laid down in these areas which may then be observed roentgenographically. They have a curvilinear, round, smooth outline and may form a complete coalescent shell about the parasite. Occasionally some deposition of lime salts may occur in the parasite itself, especially if it has died, but this is generally slight and is not of diagnostic im-

portance compared to the characteristic calcification of the fibrous capsule.

In other organs or tissues of different contrast, such as the lung or bone, the unilocular cyst may be discovered as a rounded area of increased density or as a destructive lesion. In the absence of calcification the diagnosis of echinococcus disease may be made by finding cysts from the ruptured contents. If the cyst can be reached by needle, scolices may be found in the aspirated fluid. While the hydatid is alive it produces antigens which will cause positive skin and complement-fixation tests. When death occurs the antigenic properties may be lost so that the immunologic tests may become negative. If calcification has occurred a positive diagnosis can be made from the characteristic roentgen appearance even in the absence of positive immunologic tests.

In contrast to the unilocular variety met with in all parts of the world, another less common but definite type known as the alveolar hydatid,^{1,2,5} occurs in certain geographic areas, especially southern Germany, Switzerland, Czecho-Slovakia, the Tyrol and Eastern Russia. In this type the budding germinal epithelium *evaginates* to form daughter cysts. These are more solid than the daughter cysts of the unilocular variety and contain a jelly-like substance instead of fluid. In addition, there is no distinct fibrous tissue capsule formed by the host like that which encloses the unilocular hydatid. The growth in the organs of the host is infiltrating similar to a malignant neoplasm. Buds may become seeded throughout the liver or carried to some other organ by way of blood or lymph channels. The original area of seeding may develop into a very large mass. With growth the center becomes poorly

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nourished and necrotic, and calcification may then occur. If all of the alveolar hydatid eventually dies, the whole mass may then become calcified and present itself as a large coalescent mass of irregularly calcified bodies of somewhat uniform size. The metastatic hydatids which are usually smaller may also undergo a similar type of calcification upon their death.

Because characteristic calcification of alveolar hydatids has not been generally described, the following case is reported. Although a positive diagnosis could not be established because the skin and complement-fixation tests were negative, it is felt that the type and distribution of the calcification in the liver is best explained by alveolar hydatid disease. The lack of positive immunologic tests can be explained by the complete death of the organism, with loss of antigenic properties. At any rate, the unusualness of the calcification as manifested is enough to warrant its report with the hope that it may stimulate others to report similar findings.

CASE REPORT

The patient is a white soldier, aged thirty-two. He was admitted on March 15, 1944, after having been returned from overseas. There were no specific complaints on admission. However, in February, 1942, he had been admitted to a civilian hospital because of a painless jaundice noted ten days before admission and was in the hospital for thirteen days. He was treated medically. The jaundice gradually cleared and he felt perfectly well after approximately two months. For a year before this illness, he had been in the habit of taking about ten shots of whiskey with beer as a chaser for two or three days on each week-end. At this time he ate very little food. During his treatment in the hospital a routine serological test for syphilis was positive and remained positive after the jaundice cleared. Antiluetic treatment was therefore instituted. The record from the civilian hospital revealed calcification of the liver on roentgen examination. The patient denies any knowledge of its existence. He gave no history of a primary lesion and denied any knowledge of any illness during his lifetime up to the time of his attack of jaundice. He was

born and had lived in Czecho-Slovakia until the age of nine years when he came to the United States.

On induction into the Army the serologic test for syphilis was still positive in spite of the fact that he had had some treatment. A routine course of antisyphilitic therapy was administered following his induction in the spring of 1943. During the course of his treatment he went overseas. Upon the completion of the course in December, 1943, he was admitted to an overseas General Hospital for a final check-up. The spinal fluid was found to be negative but the blood continued to be positive. A physical examination at this time revealed a hard, round mass in the epigastrium which was identified as being connected with the liver. The spleen was also found to be enlarged. Roentgen studies showed that there was a large, irregular, calcified mass in the left lobe of the liver with several smaller calcified masses scattered throughout the right lobe. Gastrointestinal studies were negative with the exception of displacement of the stomach and duodenum by the enlarged left and right lobes of the liver. Laboratory examinations at that time indicated some impairment of liver function.

Because of this enlargement of the liver and the unusual roentgenographic findings, the patient was returned to the United States for further studies.

Here, no additional facts in the history were ascertained. The physical examinations revealed no additional findings. There were no specific complaints and his general state seemed to be fairly good. The various laboratory procedures to estimate his liver function showed that the serum proteins were slightly decreased, the albumin ranging between 3.5 and 4.0 mg. per 100 cc. The cephalin flocculation test was 1 plus in forty-eight hours and another at a later date showed no flocculation. The icteric index was within normal limits. Two hippuric acid tests showed that slightly less than 1 gram of benzoic acid was excreted. All of the blood counts showed normal values for red cells and hemoglobin, but the white cell count showed a persistent leukopenia of moderate degree. The neutrophils were slightly depressed. The blood serology was again positive. The complement-fixation test for echinococcus was negative. Echinococcus antigen for skin testing was not available at this time.

Peritoneoscopy confirmed the presence of the

stony hard mass. The liver surface in addition was somewhat irregular. No biopsy was obtained because of the hardness of the mass.

Roentgenological Findings. The plain abdominal roentgenograms (Fig. 1 and 2) show a rounded 12.0 cm. mottled and irregularly calcified mass in the central portion of the upper abdomen just below the diaphragm which corresponds to the left lobe of the liver. There was no distinct calcified rim or capsule. Scattered throughout the right lobe, but somewhat more posteriorly, are similar areas of calcification. These are not arranged in any discrete mass but are irregularly distributed in the right lobe lying just anterior to the twelfth dorsal vertebra on the lateral projection and range from 1.0 to 2.0 cm. in diameter. No other calcification is noted in any other part of the abdomen. The spleen is also enlarged and extends almost to the iliac crest. The kidney shadows and psoas shadows are normal. Roentgenoscopically, no limitation of the motion of the diaphragm leaf was noted on either side.

Gastrointestinal studies showed no evidence of varix formation of the esophagus. As shown



FIG. 2. A lateral view showing the relationship of the calcified masses to the abdominal structures.



FIG. 1. An anteroposterior abdominal view showing the large coalescent, mottled, calcified mass in the left lobe and the similar smaller more discrete satellite masses in the right lobe. The enlarged spleen is also clearly outlined.

in Figures 3 and 4, the body of the stomach presented a normal contour and emptied itself readily. The antrum, pylorus, duodenal cap and proximal duodenum are displaced somewhat anteriorly by the enlarged right lobe of the liver. The distal portion of the descending duodenum and transverse duodenum are in normal position and show no displacement. No intrinsic deformity of the duodenal cap was seen. The large bowel showed no displacement.

These studies did not differ from those previously done overseas. One additional finding was suggested by the present study, and that was the presence in some of the roentgenograms of a round, circumscribed mass of tissue in the medial portion of the right liver lobe, which suggested that the liver may have contained some nodular masses of liver tissue surrounded by a connective tissue capsule.

In October, 1944, the patient was re-studied clinically and roentgenographically. No findings other than those previously described were noted. At this time a skin test with echinococcus antigen, which was obtained from the National Institute of Health, was negative. The complement-fixation test for echinococcus was repeated again and was negative. The liver function tests were again repeated. The total pro-

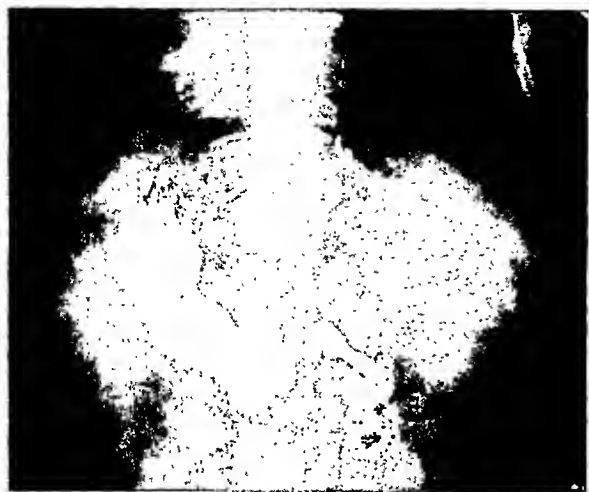


FIG. 3. Posteroanterior view showing relationship of stomach and upper small intestine to the calcified densities within the liver.

teins were 6.5 mg. per 100 cc. The bromsulfalein excretion was normal.

Infra-red photographs of the abdominal wall showed prominence of the veins supporting the evidence in favor of cirrhosis.

The patient was discharged from the hospital with a diagnosis of cirrhosis of the liver and returned to duty. It was felt that the toxins from the original lesion responsible for the calcified masses in the liver had resulted in injury to liver tissue and that in addition to the calcification of the parasite there was a nodular cirrhosis which had resulted from the liver cell damage.

COMMENT

Since calcification in liver parenchyma is so rare it was difficult to entertain a large differential diagnosis. Several possibilities were considered. Because of the positive serology a luetic cause was considered but calcification does not occur in luetic cirrhosis. Calcified hemangioma was a possibility but there was no bruit. The lack of any history of previous illness seemed to be against an abscess with subsequent calcification of the cavity. Calcification following amebic abscess is not mentioned in the textbooks of pathology. In view of the lack of any history of previous illness and the prevalence of alveolar hydatid disease in the area where this patient lived as a child until the age

of nine, it is felt that the calcification in this case is best explained etiologically on this basis. The reason for the lack of supporting immunologic data is discussed above.

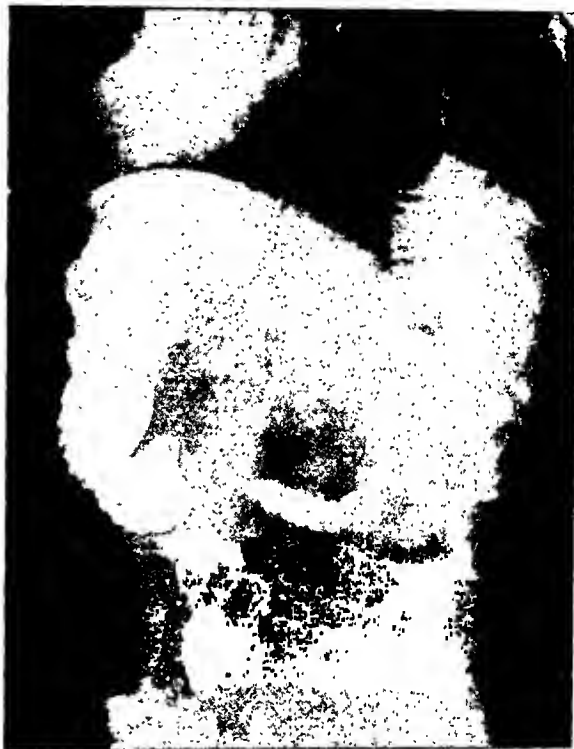


FIG. 4. Lateral view showing same relationships. Note the anterior displacement and extrinsic deformity of the proximal duodenum.

CONCLUSION

A case of unusual calcification in the liver is reported, together with a discussion of its etiology on the basis of alveolar hydatid disease.

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CONGENITAL ABSENCE OF PEDICLE FROM THE CERVICAL VERTEBRA

REPORT OF THREE CASES

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VARIOUS types of congenital anomalies are a common finding in the cervical region. These range from the block fusion of two or more adjacent vertebral bodies to the Klippel-Feil syndrome characterized by fusion of numerous segments, hemi-vertebrae, spina bifida, scoliosis and other deformities. These disturbances of segmentation probably arise in the blastemal or chondral periods of development within the first eight weeks of fetal life.

Another congenital condition, atlanto-occipital fusion, with or without platybasia, may be the cause of neurological symptoms from constriction of the foramen magnum. Foramen distortion may result also from cervical vertebra, a case of which I have previously reported.¹

Absence of the pedicle is not rare but may remain unrecognized or be misinterpreted and thus cause confusion, especially following an accident. For that reason, the following 3 cases are reported. Case I was briefly described in a previous communication.²

The sine quo non is a good pair of stereoscopic 45° oblique studies made with the patient either prone or upright.

REPORT OF CASES

CASE I. A physician, aged thirty-five, forced off the road by a sleepy truck driver, was thrown from his car when it struck a tree. Pain in the neck was only slight, and there was no muscle spasm. There was some limitation of motion, however, upon extreme rotation of the head toward the left. The patient's mother stated that to her knowledge he had never sustained any previous injury. Roentgenograms were at first believed to show a dislocation or a compression fracture although the patient's clinical appearance did not confirm it.

Further roentgen studies of the cervical region, however, were reported as follows: The right side appears normal except for a small

fifth foramen and increased density of the fifth arch. On the left side, there is a complete absence of the fifth pedicle with a large foramen at this level. The fourth pedicle is more slender than normal. The cortex of the fifth arch is more dense than the fourth or sixth and lies posterior to their plane. The left sixth superior articular process is somewhat enlarged, and its articulation with the fifth is posterior and above normal position. From this point, the fifth superior articular process extends upward to about $\frac{1}{8}$ inch from the posterior surface of a large, dense fourth inferior articular process rather than articulating with its anterior surface in the normal manner. The customary articular plane slanting from above downward and backward is absent between the fourth and fifth. The fifth transverse process arising from the body in front is well developed but seems to be unattached posteriorly. There is a hyperplasia of the upper left lateral margin of the fifth vertebral body articulating with the fourth body above for greater stability. The flexion extension studies show no localized limitation of movement. There was some list of the cervical spine toward the left side.

CASE II. Female, aged seventy-seven; no history of accident but she complains of pain in the cervical region. Oblique study shows a complete absence of the fifth pedicle on the right side with a long foramen extending from the fourth to the sixth pedicle. A rudimentary transverse process extends backward from the lower margin of the fifth vertebral body toward the fifth and sixth posterior articulation. This divides the large foramen into a middle and a smaller lower portion. A spur from the degenerated fourth disc projects backward into the upper part of the foramen. This upper portion is further encroached upon by the fifth superior articular process which has subluxated forward into it. The entire fifth neural arch is intact. The slender left side of it is to be seen crossing the middle portion of the foramen behind the fifth body. This must not be mistaken for the pedicle.

This patient has advanced intervertebral

disc degeneration with thinning and spur formation of the disc margins. Bony bridging is particularly heavy between the fourth and fifth bodies, doubtless for additional stability. Flexion extension studies show almost complete fixation between all cervical segments below the first and second articulation. There is only a very slight list toward the right side, and rotation is limited.

CASE III. This patient, male, aged forty-one, believes condition of neck resulted from a foot-

are painless but limited to less than one-half normal. These movements are somewhat more free toward the left side but produce pain referred down the arm.

Roentgen studies show absence of the third right pedicle. The large foramen extends from the second to the fourth pedicle, but on the roentgenogram it is partially obscured by the rudimentary transverse process arising from the third vertebral body. The right half of the third neural arch is absent, and the left half

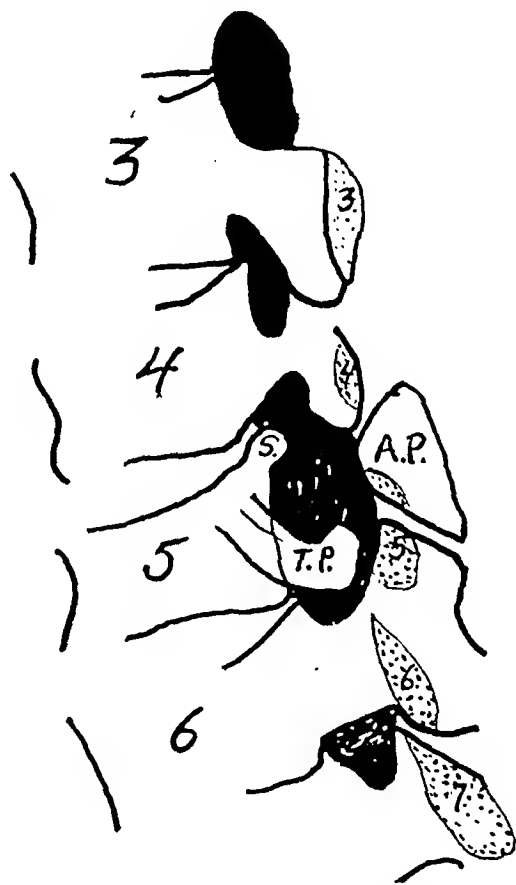


FIG. 1. Case I. Vertebral bodies numbered. Large foramen where fifth left pedicle is missing. The bony shadow overlying this foramen is the right side of the neural arch. *T.P.*, transverse process; *S.*, stabilizing hyperplastic spur articulating with fourth body above. Profiles of the left sides of the neural arches are stippled. *A.P.* is the fifth upper and lower articular processes partly overlying the fifth neural arch.

ball injury in early life. Pain has become troublesome since straining left shoulder and neck six months ago. The head is held to the left side, and all subjective symptoms are on the left. Besides pain, there is limitation of motion and numbness of the thumb and first finger. The left trapezius muscle is spastic. Rotation and flexion of the neck to the right

terminates in a small spinous process. There is some rotation of the second segment with its spinous process displaced toward the right.

Along with the absent pedicle, there are on the right side no articular processes for the third segment. There is, however, a large articular process extending from the second cervical body downward and a somewhat similar mas-

sive articular process extending from the fourth body upward to articulate with it. These bypass the third body completely. The plane of

each one an enlarged intervertebral foramen was visualized on the 45° oblique roentgenogram.

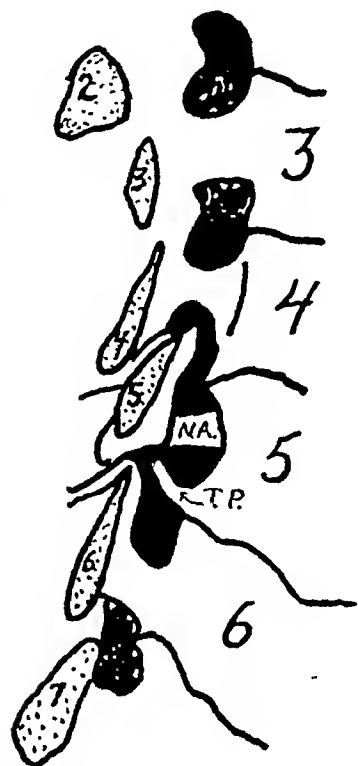


FIG. 2. Case II. Large foramen extending from fourth to sixth pedicle. Fifth right pedicle missing. *N.A.* is the slender left side of the fifth neural arch. This is not the pedicle. *T.P.* indicates the rudimentary transverse process. Encroachment of second foramen by spur from posterior articulation. Encroachment of sixth foramen by spur from degenerated disc. The fifth neural arch (stippled) is displaced forward and upward from its normal alignment with the other arches thereby constricting the upper part of the large foramen. Compare this with the diagram of Case I (Fig. 1) where the involved arch is displaced backward from its normal alignment with the other arches resulting in a foramen much larger in its anteroposterior diameter.

this second-fourth articulation is horizontal. It lies well anterior to the normal posterior articulations, so that when the neck is dorsally extended, its articular surfaces become widely separated but resume contact again upon anterior flexion. There is a distinct list of the spine toward the left side but relatively good movement between the cervical segments.

DISCUSSION

From a study of these 3 cases of absent cervical pedicle, it will be noted that in

The transverse processes were deficient posteriorly. Except in Case II with advanced arthritic changes, movement was relatively free but with some limitation of rotation toward the affected side. The condition per se does not seem to be painful; symptoms in Case II were probably arthritic, and Case III was complaining of pain on the opposite side following injury six months before. The fifth left and the fifth and third right pedicles were missing respectively.

It is interesting to observe how compensation for the resultant weakness was effected. In Case I, the neural arch became more dense and a hypertrophic bone process extended from the margin of the involved vertebral body to that above. Case II developed a heavy bony bridging between the deficient vertebra and the one

light, let us consider the matter of early development.

Embryologically,³ the vertebral segments each develop from three paired centers. These first appear in the blastemal or membranous stage but become well elaborated during the chondral stage before the end of the second fetal month. There are

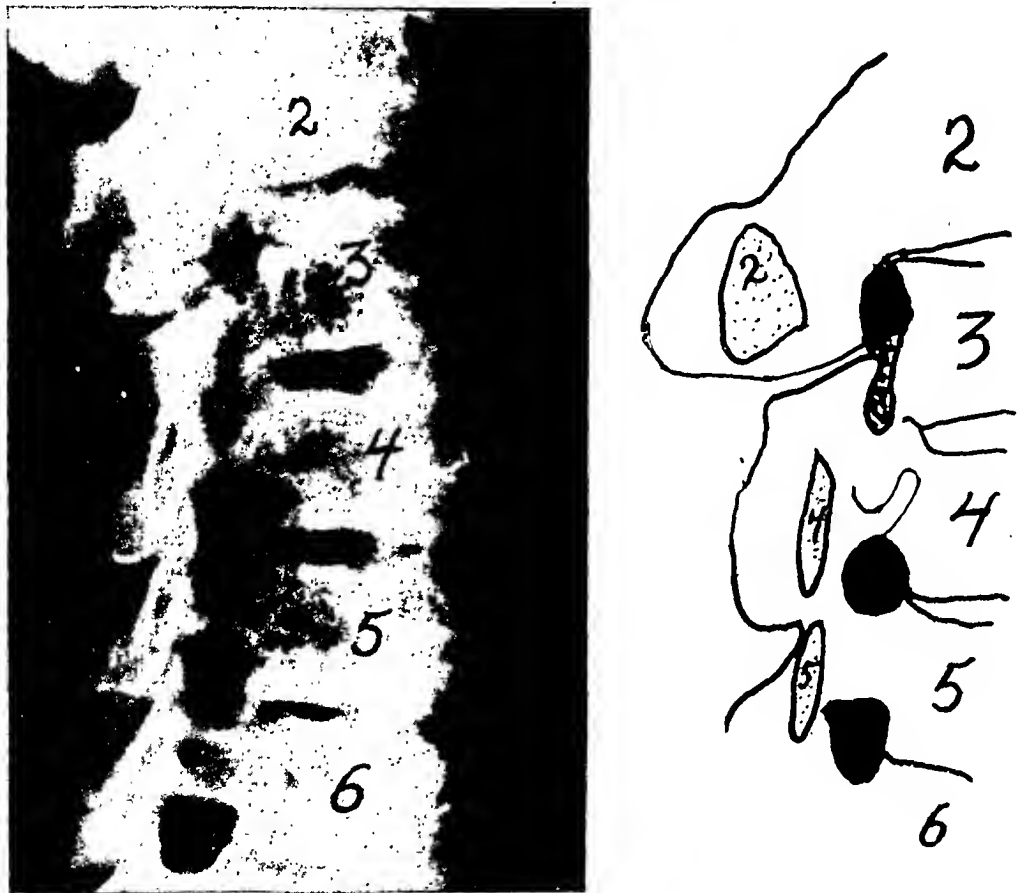


FIG. 3. Case III. Third right pedicle missing. Foramen extending from second to fourth pedicles partly overlaid by third transverse process. Large horizontal articulation between massive second and fourth articular processes. Third neural arch missing, right side (see stippled areas).

above, while in Case III, a strong bony column extended from the vertebra above to the one below, completely bypassing the weaker vertebra.

In both Cases I and II, the complete neural arches were present and likewise the posterior articulations on the involved side, although one of them was distorted. In Case III, half the neural arch and the articular processes of the weakened side were absent along with the pedicle. In this

six centers of chondrification, two for the vertebral body, two costal centers for the ribs and one for each side of the neural arch. From each neural arch center, outgrowths develop to form the pedicle, the superior and inferior articular processes, the transverse process and the lamina with its spine.

Ossification begins about the third fetal month. There is usually one center (rarely, two) for the vertebral body and one for



FIG. 4. Case 111. Massive second-fourth articulation on right side. N.A., left side of neural arch. Profile of pedicles stippled. Patient has no third pedicle, articular processes or neural arch on right side.

each side of the neural arch. The ribs ossify separately, but in the cervical region, the early chondral rib element remains attached to the vertebral body and joins the early transverse process element to enclose the vertebral artery. This forms the adult type of cervical transverse process.

In the light of this brief statement, it is interesting to evaluate the deficiencies observed in the 3 cases here reported.

In Case 111, there was a complete absence of all elements arising from the cartilaginous neural arch center. In Cases 1 and 11, while the pedicle was absent, the lamina and the articular processes had developed, although one of these was deficient in Case 1. The transverse processes seemed deficient posteriorly and doubtless originated only from the costal element attached to the vertebral body.

SUMMARY

Congenital absence of the pedicle in the cervical region may be visualized by the 45 degree oblique roentgenogram. There is a resultant enlargement of the intervertebral foramen at this level. This opening may be partially obscured by an overlying transverse process, an exostosis or the lamina on the opposite side.

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THE PROTECTION OF PHOTOFLUOROGRAPHIC PERSONNEL*

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THE widespread use of mass roentgenographic methods in the examination of the chest has introduced several new problems in the field of radiation protection. Operating schedules of photofluorographic equipment frequently exceed five hundred exposures per day, a rate considerably greater than that encountered in general roentgenography. Furthermore, Birnkrant and Henshaw¹ have recently shown that the quantity of radiation required for the exposure of a photofluorographic film is approximately eighteen times greater than that needed for the exposure of a conventional 14×17 inch roentgenogram. It is therefore evident that the radiation hazard to which the personnel of a mass roentgenographic installation are subjected is considerable and that adequate protective measures must be provided to prevent serious radiation injury.

Before protective equipment may be intelligently designed for a roentgen installation, the radiation intensity which prevails in the vicinity of the unit during exposure must be known. In addition, absorption data for a variety of protective materials and pertinent to the range of radiation quality which is expected should be available. Birnkrant and Henshaw have measured the quantity of radiation received at several locations about a photofluorographic unit. The small number of measurements that were taken, however, limits considerably the applicability of their data in many design problems. A small amount of data regarding the absorption of various protective materials under photofluorographic conditions is also available but this, too, is useful only under limited conditions. In an effort to obtain more comprehensive information

radiation measurements have recently been conducted on a photofluorographic installation in this laboratory. Sufficient data were obtained to permit the plotting of isodose curves from which the radiation intensity at any location within a large field surrounding the unit may be determined. In addition, absorption curves for lead, iron, aluminum and Masonite presdwood were obtained under actual photofluorographic conditions.

The photofluorograph used in the investigation was a standard 35 mm. Westinghouse model, equipped with a grid and located in the center of a large room, 45 feet long, 35 feet wide and 12 feet high. Floor and walls were of concrete and plaster construction with no wooden structures from which spurious scattered radiation could emanate when impinged upon by the direct roentgen-ray beam; the ceiling was of sheet steel.

The study was initiated by measuring the quantity of radiation received at a number of widely scattered locations within the enclosure when a subject whose chest measured 24 cm. in thickness was photofluorographed with the roentgen machine operating at 100 kv. (peak), 200 ma. and with an exposure time of 0.15 second; measurements were made with a Victoreen ionization chamber having an air capacity of 100 cc. The procedure was then repeated using tempered presdwood phantoms of gradually increasing thickness until the quantities of radiation measured at the several locations were equal to those occurring when the 24 cm. subject was placed in the beam. The phantom which produced an equivalent effect to that of the subject was one 12.5 cm. in thickness and having a surface normal to the roentgen beam, 40

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by 40 cm.* Thereafter throughout the investigation such a phantom was used instead of the human examinee as a scattering agent.

The quantity of radiation to which one is exposed within a photofluorographic room under normal operating conditions was determined by measuring the roentgen intensity at 18 inch intervals throughout the test enclosure when the roentgen tube was operated at 100 kv. (peak) and 25 ma. Ionization measurements were made with a 100 cc. chamber whose ionization current was amplified by a highly stable and highly sensitive vacuum tube circuit.² Such an arrangement was sufficiently sensitive to permit the accumulation of readings with but one exposure per location and with the roentgen tube operating under conditions which allowed the rapid recording of data from the large number of locations studied without excessive heating of the tube. The readings taken in this way of course indicate only the roentgen intensity received under the special conditions of the test and require conversion to roentgens per normal photofluorographic exposure before they become useful. Such conversion was obtained by multiplying the data by a factor derived in the following manner: The quantity of radiation received at a particular location was measured by conventional procedure when an exposure was made in which the roentgen tube operated at 100 kv. (peak) and 30 mas. (the exposure previously found to produce a photofluorogram of optimum density of the 24 cm. subject). A reading was then made with the chamber-amplifier apparatus at the same location with the roentgen tube operating at 100 kv. (peak) and 25 ma. The ratio of the first reading to the second represents the desired conversion factor.

The ionization chamber with which all of the foregoing data were obtained was

constructed of bakelite having a wall thickness of 1.8 mm. The absorption of such a thickness of bakelite when tested with the scattered radiation produced by the phantom was slightly less than 5 per cent. Accordingly, the various results were multiplied by an additional factor of 1.05 to correct the readings to so-called "air-wall" conditions.

The results of the investigation are illustrated graphically in Figure 1 where the quantities of radiation received at various locations about a photofluorograph are charted. The data expressed in roentgens per one hundred exposures are plotted as isodose curves. These data apply not only in the horizontal plane as shown but in any plane located radially about the longitudinal axis through the photofluorograph. Thus the radiation conditions occurring in rooms above and below the unit may be derived merely by locating on the chart the position of the rooms relative to the photofluorograph and reading the dosage rate at that point. For example, the quantity of radiation to which an individual is subjected when located in a room 9 feet directly above the roentgen tube is slightly less than 0.014 r per one hundred exposures.

The contours of the several isodose curves are of considerable interest. Directly behind the roentgen tube the dosage rate is relatively low, and rises to rather high levels as one progresses laterally. Also at a position directly lateral to the photofluorographic screen there is a sharp change of curve configuration with a progressive diminution of the dosage rate as one advances to the left parallel to the photofluorographic camera. These phenomena point unmistakably to the conclusion that the radiation to which operating personnel are exposed within the photofluorographic enclosure is scattered radiation originating within the subject under examination. Behind the roentgen tube this radiation is of relatively low intensity because of the shielding which the tube affords. Similarly, the dosage rate in the region of the photofluorographic camera is extremely low

* The equivalence of the radiation measurements made with this phantom on the one hand and the subject on the other was surprisingly close at the several locations not only when the tests were made at a single kilovoltage but when the procedure was repeated at 80 and at 90 kv. (peak), and with and without the use of a beam-limiting cone.

because of the very considerable shielding which the large photofluorographic hood provides. The sharp change in the contour of the curves which occurs lateral to the hood may also be ascribed partly to the shielding of the hood and also to the shielding of the subject's lateral tissues which fall outside the direct beam and therefore have a small shielding effect. Where there is no shielding, i.e. along a line extending pos-

to 50 per cent greater than that needed for the exposure of 35 mm. film. Accordingly, the dosage rates are correspondingly greater than those shown in Figure 1 for such equipment.

(b) Other types of patients: A subject 24 cm. in thickness was deliberately chosen for this study because such an individual is somewhat larger than average and accordingly the data so obtained will tend

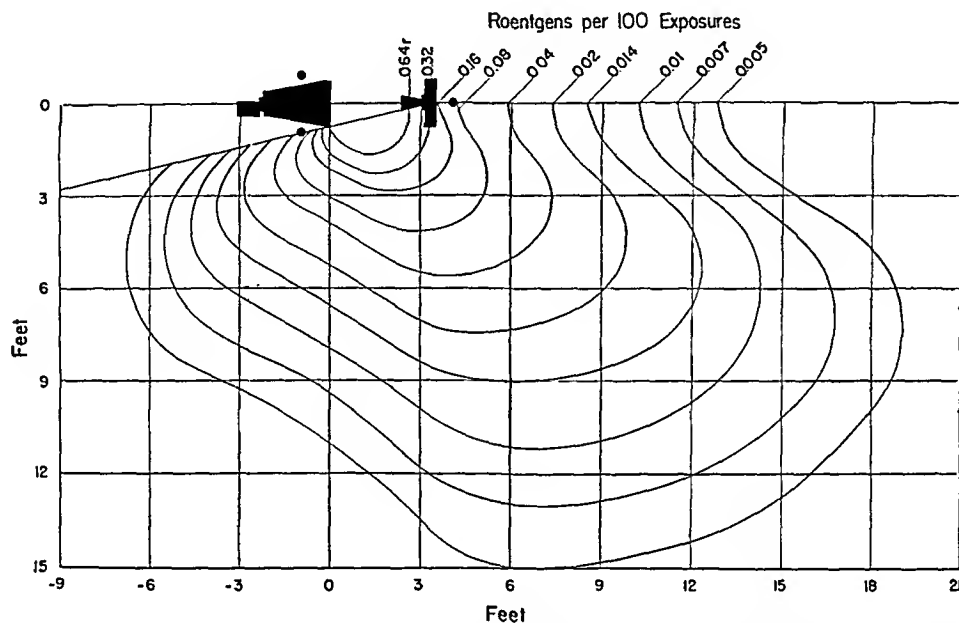


FIG. 1. Isodose curves illustrating the exposure conditions which exist about a photofluorographic installation. Data indicate the quantity of radiation, in roentgens, received per one hundred exposures at various locations about the unit.

teriorly and laterally from the subject, the dosage rates are relatively high.

The data illustrated in Figure 1 apply strictly only to a 35 mm. photofluorograph, roentgenographing patients 24 cm. in thickness, with the roentgen tube operating at 100 kv. (peak), with a cone limiting the roentgen beam, with a grid incorporated in the photofluorographic hood and with scattering material within the enclosure reduced to a minimum. Under other operating conditions the data will be modified in the following manner:

(a) Other types of photofluorographic equipment: The quantity of radiation required for the exposure of 70 mm. and 4 by 5 inch photofluorograms is from 25

to present values somewhat greater than those normally encountered. A desirable factor of safety will thereby be introduced.

(c) Other roentgen tube voltages: When measurements were made with roentgen tube potentials of 90 kv. (peak) and 80 kv. (peak), dosage rates respectively 20 per cent and 40 per cent higher than those obtained at 100 kv. (peak) were obtained. These observations may seem somewhat paradoxical because it is well known that scattered radiation originating within a medium diminishes as the roentgen tube potential decreases. Actually, measurements of roentgen intensity indicated just such a diminution but the exposure times required for the production of photofluoro-

grams of optimum quality were prolonged to such an extent when the kilovoltage was lowered that the quantities of radiation increased by the amounts listed above.

(d) Conditions when a cone, limiting the roentgen beam, is absent: Birnkrant and Henshaw¹ have reported an increase in the dosage rates of from 27 to 48 per cent when a limiting cone is not used. Measurements made during this investigation confirmed these observations and revealed an average increase of 30 per cent.

(e) Conditions when a grid is not incorporated in the photofluorograph: The absence of a grid decreases the average photofluorographic exposure by approximately 50 per cent with a corresponding diminution in the dosage rates. Since conventional practice demands the use of a grid routinely in order to improve film quality, this fact is hardly of sufficient significance to bear notation.

(f) Conditions when the walls of the photofluorographic enclosure receive the direct roentgen beam: When the direct roentgen beam falls on the walls of the photofluorographic room, the dosage rates will be increased. This effect will be particularly marked when the walls are of wooden or cellulose construction. Dosage rates, 50 to 100 per cent higher than those shown in Figure 1, were observed opposite the photofluorographic hood and camera in the peripheral portions of the enclosure when a wooden wall, $\frac{1}{2}$ inch in thickness, was placed behind and to the side of the camera. This effect of course may be easily eliminated by restricting the roentgen beam with a lead-impregnated flange of relatively small dimensions surrounding the photofluorographic hood immediately behind the plane of the screen.

Although the information provided by Figure 1 is of considerable interest it does not permit the design of protective screens for use in photofluorographic installations without absorption data on available protective materials. As a part of the current investigation, absorption curves were obtained on lead, steel, aluminum and

Masonite presdwood. These curves were derived from measurements made with the ionization chamber-amplifier circuit used in obtaining the dosage rate data and with radiation scattered from the 12.5 cm. presdwood phantom when irradiated with a roentgen tube operating at 100 kv. (peak). This radiation therefore was identical in quality to that encountered in actual photofluorographic practice. In these studies, the ionization chamber was en-

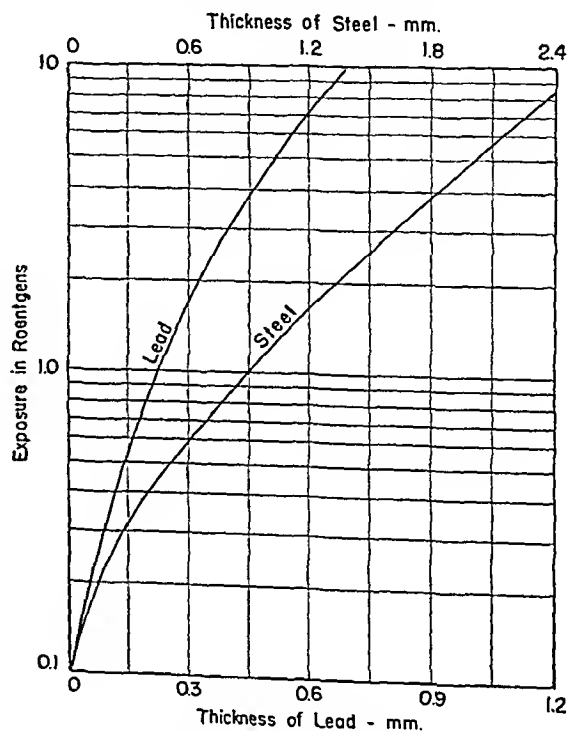


FIG. 2. Thicknesses of lead and steel required to reduce various quantities of radiation received about a photofluorographic installation to 0.1 r.

closed in a lead container, in one side of which was a portal, 10 by 15 cm., which restricted the entrance of radiation to that emanated by the phantom.

The absorption data for lead and steel are plotted in Figure 2, where the thickness of lead and steel required to reduce the quantity of radiation received at any location to 0.1 r is plotted against the dosage received at that location. For example, if the quantity of radiation received at a particular position is 1.0 r, it will be reduced to 0.1 r by 0.22 mm. of lead or 0.9 mm. of steel.

The maximum daily dose of roentgen radiation which may be tolerated by an individual operating roentgen equipment has been arbitrarily established at a level of 0.1 r per day.³ From Figures 1 and 2, then, the minimum requirements for the construction of photofluorographic protective screens may be easily calculated for any location in which operating personnel may wish to work. For example, an unprotected person working immediately behind the roentgen tube of a photofluorograph which has an average operational rate of five hundred exposures per day would receive 0.40 r per day (i.e., 0.08×5 r per day). Reference to Figure 2 indicates that the protective screen at this location should include lead at least 0.1 mm. in thickness, or steel 0.4 mm. in thickness.

The relatively small thicknesses of lead and steel which are required for adequate protection has prompted some people to consider aluminum as a protective material. Absorption measurements, however, indicate that a thickness of aluminum approximately ninety times that of lead is required for equivalent absorption. The use of aluminum is therefore not feasible economically nor from the standpoint of weight.

Absorption measurements of Masonite presdwood (density=1.07) indicate that

the absorption of this material is less than 0.1 per cent of that of lead. It is therefore apparent that persons working in rooms separated only by wooden or cellulose walls, floors or ceilings from a photofluorographic installation require serious consideration when the problems of protection are considered. When the separating partitions are of concrete (density=2.4) or brick the absorption of these materials will be approximately 1.0 per cent and 0.5 per cent respectively of lead.⁴ It is unlikely then that when these building materials are used any added protective measures will be required, unless the wall is impinged upon by the direct roentgen-ray beam, since the thickness of partitions made with these materials usually exceeds 2 to 4 inches.

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THE CALCULATION OF DOSE FROM POINT AND LINEAR SOURCES OF RADIUM*

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METHODS for the calculation of dose from point and linear sources of radium have been published by several physicists. These methods all possess a high degree of accuracy but are somewhat complex in their practical application. It is therefore of advantage to group together the pertinent data and to simplify the physical formulas to a point consistent with the accuracy permitted by our present knowledge of the subject and our limited technical facilities.

The calculation of dose in gamma-ray therapy depends upon the fundamental rule that the intensity of gamma radiation from a point source of radium varies inversely as the square of the distance from the source and directly as its strength. The dose at any given point is equal to the product of the intensity at that point and the time of application.

$$I \propto \frac{M}{h^2}$$

$$D = I \times t$$

where I = intensity at point Q (Fig. 1),
 M = strength of radium source, usually measured in milligrams,
 h = distance of Q from M , usually measured in centimeters,
 D = dose at point Q ,
 t = time of application, usually measured in hours.

The gamma roentgen, r_r , is now generally accepted as the unit of dosage in radium therapy. The relation between the gamma roentgen and the strength of a radium source is given in the rule that the intensity of gamma radiation 1 centimeter from a 1 milligram point source of radium filtered by 0.5 millimeter of platinum is 8.4 gamma roentgens per hour. This value may

be termed the gamma roentgen conversion factor for gamma rays of radium filtered by 0.5 millimeter of platinum. The conversion factors for other filters may be calculated from the absorption formula:

$$C = 9.0 \times e^{-ud}$$

where C = conversion factor,
 u = absorption coefficient of gamma rays of radium in filter used,
 d = thickness of filter.

The conversion factors for the more com-

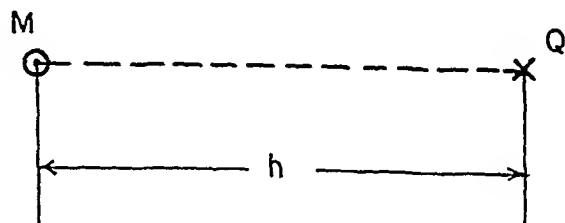


FIG. 1.

monly employed filters of platinum, calculated from this formula, are given in Table I. These factors apply only to gamma radiation. The effects of primary and secondary beta radiation are not considered. With a primary filter of 0.5 mm. platinum, or 1.0 mm. lead, or 2.0 mm.

TABLE I
CONVERSION FACTORS FOR VARIOUS PLATINUM
FILTERS OR EQUIVALENT

Thickness of Platinum Filter	Conversion Factor— C
0.0 mm.	9.0
0.3 mm.	8.6
0.5 mm.	8.4
0.6 mm.	8.2
0.8 mm.	8.0
1.0 mm.	7.7
1.5 mm.	7.2
2.0 mm.	6.7

* From the Department of Radiotherapy, Mount Sinai Hospital, New York.

TABLE II
PLATINUM-EQUIVALENT FACTORS FOR VARIOUS
METALS AND ALLOYS

Metal or Alloy	Platinum- Equivalent Factor
Platinum	1.0
Platinum-iridium	1.0
Gold	1.0
Lead	0.5
Silver	0.45
Nickel	0.25
Copper	0.25
Monel metal	0.25
German silver	0.25
Brass	0.25
Steel	0.22
Tin	0.22
Zinc	0.22
Aluminum	0.1

brass, practically all of the primary beta radiation is absorbed.

The amount of secondary beta radiation originating in the primary filter is at a minimum with elements of intermediate atomic number, such as steel, nickel, copper, zinc or tin. Quimby, Marinelli and Blady have shown that these elements produce less secondary beta radiation than elements of high atomic number, such as lead, gold or platinum, or those of low atomic number, such as hydrogen, carbon, oxygen, and so forth, which are found in rubber, wax, bakelite, and similar substances. The secondary beta radiation is absorbed almost entirely in the first 1 or 2 millimeters of tissue.

If other metal filters are employed instead of or in combination with platinum, the conversion factors can be calculated from the absorption formula. However, an approximation sufficiently accurate for radium therapy may be obtained by an estimation of the thickness of platinum which gives the same amount of absorption of gamma rays as the thickness of metal used. The platinum-equivalent thickness

may be determined by multiplying the thickness of the filter by its platinum-equivalent factor, which is given in Table II.

The factor of absorption in tissue and similar substances, such as wax, wood, water and lead-free rubber is complicated by an increase of radiation due to scatter. The exact value in any particular case can be determined only by actual measurement. However, from data published by Failla, Laurence, and Sievert, an approximation sufficiently accurate for radium therapy can be made. This is best expressed in the form of a factor (S) for varying thicknesses of tissue, as given in Table III.

From this data, the "point source formula" may be derived for the dose in gamma roentgens delivered by the gamma radiation from a point source of radium at any given distance.

$$D = \frac{M \times t \times C \times S}{h^2} \quad (1)$$

where D = dose in gamma roentgens at point \mathcal{Q} (Fig. 1),

M = milligrams of radium,

t = hours of application,

C = conversion factor for filter used,
 S = tissue factor (if radiation is in air, this factor = 1.0),

h = distance in centimeters between the radium source and point \mathcal{Q} .

TABLE III

TISSUE FACTORS FOR VARIOUS THICKNESSES OF TISSUE

Thickness of Tissue	Tissue Factors— S
1.0 cm.	0.98
2.0 cm.	0.95
3.0 cm.	0.94
4.0 cm.	0.93
5.0 cm.	0.92
7.0 cm.	0.89
10.0 cm.	0.84
15.0 cm.	0.75
20.0 cm.	0.67

Conversely, the number of milligram-hours of radium (or millicurie-hours of radon) required to deliver a specified dose in gamma roentgens at any given distance from the point source may be calculated from the same formula.

If radon is used instead of radium, the equivalent number of millicurie-hours may be calculated from the radon disintegration formula if radon decay tables are not available:

$$M \times t = Mc \times [1 - e^{-0.00755t}] \times 133$$

where $M \times t$ = equivalent number of millicurie-hours,

Mc = number of millicuries at beginning of application,

t = time of application, in hours.

For permanent implants, the exponential factor becomes zero.

$$M \times t = Mc \times 133.$$

If the permanent implants are in the form of gold or platinum seeds with a wall thickness of 0.3 mm., a useful modification of the point source formula may be derived for

needle or a tandem, may be derived mathematically from the point source inverse square law. In any linear source, the active length must be known. If several sources are used in a line, the over-all active length should be measured. In Figure 2, the active length of this 2.2 cm. capsule is 1.6

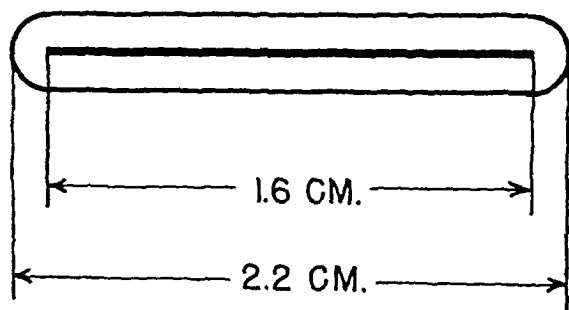


FIG. 2.

cm., whereas, in Figure 3, the over-all active length of a tandem of three such capsules is 6.0 cm.

For the derivation of the formula, it is essential that the radium be evenly distributed; that is, the linear density, or the number of milligrams of radium per centi-

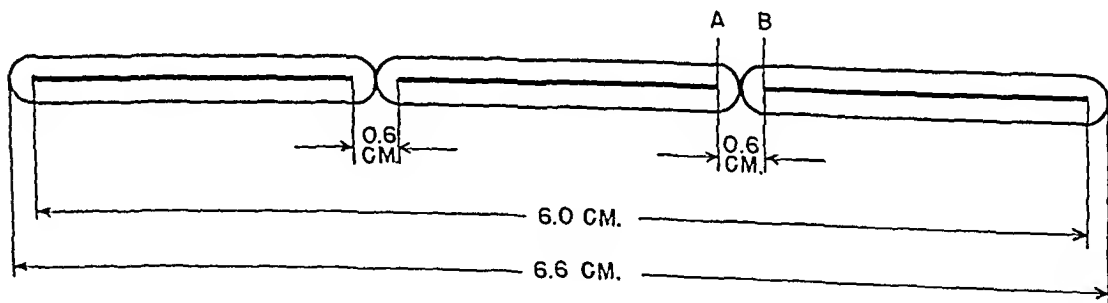


FIG. 3.

the number of millicuries required to deliver 1,000 r_r at any given distance.

$$Mc \text{ per } 1000 \text{ r}_r = \frac{1000 \times h^2}{133 \times 8.6} = 0.88 \times h^2. \quad (1A)$$

In this formula the factor for tissue absorption is not included since it is slight for the range of activity generally required of seeds.

A formula for the calculation of dose from a linear source of radium, such as a

meter, should be uniform. Where a linear source is made up of several capsules or needles in a line, as illustrated in Figure 3, the inactive gaps, *AB*, should be made as small as possible. An inactive gap equal to "0.5 *h*" (see Fig. 4 for definition of "*h*") introduces an error of 5 to 10 per cent.

The basic method of calculation of the dose from a linear source is the division of the active length into a number of small segments. The contribution to the total

TABLE IV
 RATIO FACTORS FOR VARIOUS FILTRATIONS OF PLATINUM OR EQUIVALENT

Ratio		Ratio Factor— f (ratio)				
$\frac{L-a}{h}$	$\frac{a}{h}$	$f \frac{L-a}{h}$	$f \frac{a}{h}$	$f \frac{L}{h}$	or	$f \frac{L}{2h}$
$\frac{L}{h}$ or $\frac{L}{2h}$		No Filter	0.5 mm. Pt	1.0 mm. Pt	1.5 mm. Pt	2.0 mm. Pt
10.0		13.22	11.45	10.00	8.84	7.82
8.0		13.01	11.34	9.95	8.78	7.81
6.0		12.65	11.12	9.82	8.73	7.77
5.0		12.36	10.93	9.69	8.65	7.71
4.5		12.17	10.78	9.60	8.58	7.67
4.0		11.93	10.62	9.48	8.49	7.60
3.5		11.64	10.40	9.31	8.35	7.50
3.0		11.24	10.09	9.06	8.17	7.34
2.5		10.71	9.67	8.72	7.90	7.12
2.0		9.96	9.04	8.21	7.47	6.76
1.8		9.57	8.71	7.93	7.22	6.55
1.6		9.11	8.31	7.58	6.93	6.30
1.5		8.84	8.07	7.37	6.75	6.15
1.4		8.57	7.82	7.15	6.55	5.98
1.3		8.25	7.53	6.90	6.34	5.79
1.2		7.88	7.23	6.63	6.09	5.57
1.1		7.50	6.88	6.32	5.81	5.33
1.0		7.07	6.49	5.98	5.51	5.05
0.9		6.60	6.07	5.59	5.16	4.74
0.8		6.08	5.59	5.16	4.76	4.39
0.7		5.50	5.07	4.68	4.34	3.99
0.6		4.86	4.49	4.15	3.83	3.54
0.5		4.17	3.85	3.56	3.27	3.05
0.4		3.43	3.16	2.93	2.71	2.51
0.3		2.62	2.42	2.25	2.08	1.93
0.2		1.77	1.65	1.53	1.42	1.31
0.1		0.90	0.84	0.77	0.72	0.67

that is, as x varies from $-a$ to $L-a$. The integration was performed graphically by Sievert. The "linear source formula" may therefore be written in the following form:

$$D = \frac{M \times t}{L \times h} \times \left[f \left(\frac{L-a}{h} \right) + f \left(\frac{a}{h} \right) \right] \times S \quad (2)$$

where D is the dose in gamma roentgens.

The expressions, $f[(L-a)/h]$ and $f(a/h)$, represent functions which take into account the effect of oblique filtration and the effect of the varying distance of the point from successive minute segments of the linear source. Since it is a ratio that is involved, i.e. length of the source to distance of the point from the source, the

formula holds for any length of source and any distance (except zero). The values of these functions may be calculated from Sievert's data and are given in Table IV for the more commonly employed filtrations of platinum or equivalent and for ratios varying from 10:1 to 1:10. The values for other filtrations of platinum and for ratios intermediate between those given in the table may be obtained by interpolation. These values may be called "ratio factors." The ratio factors have been calculated so that the formula reads directly in gamma roentgens.

Ratios greater than 10:1 are seldom encountered in radium therapy whereas

for ratios less than 1:10, the point source formula is equally as accurate and simpler to use. For a ratio of 1:3, the error involved in using the simpler point source formula is about 5 per cent. Therefore, for practical purposes, a linear source may be considered as a point source if the distance at which the dose is determined is more than three times the length of the source.

The tissue factor, S , to be used in the linear source formula may be obtained from Table III for the distance h . This distance is a suitable average for the

at any given point may be calculated from the linear source formula.

The ratio factors may also be used to estimate the relative doses at points along a line parallel to the linear source. The doses in the midplane, i.e. at point Q_1 , Figure 5, are always maximum for any given distance h

$$\frac{D \text{ at point } Q_2}{D \text{ at point } Q_1} = \frac{f\left(\frac{L-a}{h}\right) + f\left(\frac{a}{h}\right)}{2f\left(\frac{L}{2h}\right)}.$$

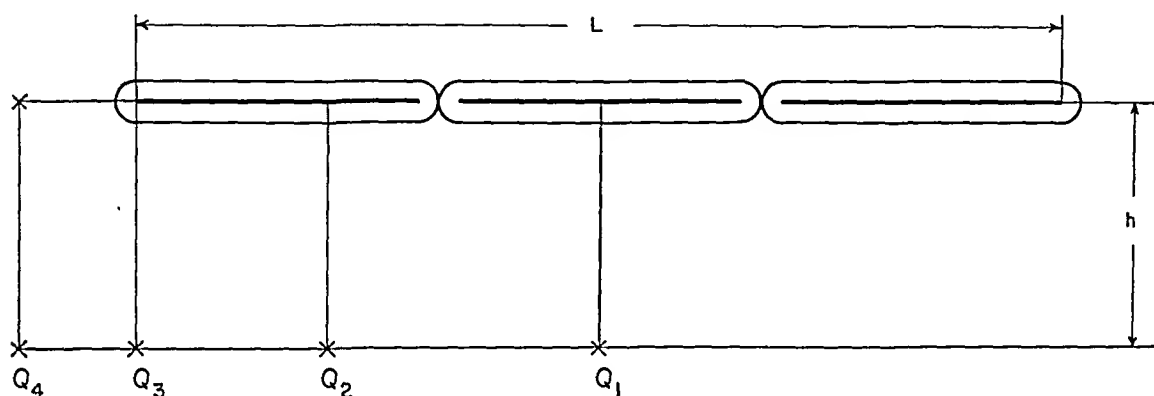


FIG. 5.

effect of tissue absorption, since the tissue factor is, at best, a rough approximation.

For points beyond the end of the linear source, e.g. point Q_4 , Figure 5, the segment a is the length of the extension from line L to the perpendicular from the point. Algebraically this segment is negative. Therefore, when its value is substituted in the linear source formula, the proper algebraic sign must be observed (see example 2 D).

For points (Q_1 , Fig. 5) in a plane at right angles to the midpoint of the linear source, a equals $L/2$. The ratio factors are therefore simplified to $2f(L/2h)$. Similarly, for points (Q_3 , Fig. 5) in a plane at right angles to one end of the linear source, a equals zero, and the ratio factors are therefore simplified to $f(L/h)$.

Conversely, the number of milligram-hours of radium (or millicurie-hours of radon) required for a linear source to deliver a specified dose in gamma roentgens

DISCUSSION

The point and linear source formulas, while mathematically accurate, are based upon certain assumptions and factors which limit their accuracy in practical radium therapy.

The formulas are based upon a theoretical point or line without thickness. An error is therefore introduced because of the dimensions of the radium source. Radium seeds are generally regarded as point sources but they usually measure 3 to 4 mm. in length. A needle or capsule may have an inner diameter varying from 0.5 to 1.5 mm. Since distance measurements are made from the central axis of the source, calculations for points closer than 0.5 cm. are subject to a large error. For distances greater than 0.5 cm., however, the error is small enough to be disregarded. Another source of error lies in the possible uneven distribution of the radium in the needle or capsule. This can sometimes be demon-

strated in an autoradiograph.

The conversion factors depend upon the values of the absorption coefficients, except the factor for 0.5 mm. of platinum which was obtained experimentally. The experimental values for this filtration range between 8.0 and 8.6. The value of 8.4 appears to be the mean and is therefore accepted for this article. There are no "accepted" values of the absorption coefficients. Kohlrausch found the absorption coefficient for platinum to be 2 cm.⁻¹, Mayneord and Honeyburne 1.5 cm.⁻¹, and Laurence 1.39 cm.⁻¹. Laurence states that the value obtained by Kohlrausch cannot apply to radium therapy because the effect of scattered radiation from the filter was not considered. For this article, the value of 1.5 cm.⁻¹ was accepted arbitrarily and used in the calculation of the conversion factors in Table I. The differences between these values and those obtained by employing a coefficient of 2 cm.⁻¹ or 1.39 cm.⁻¹ are given in Table v.

For metals other than platinum, the absorption coefficients obtained by Laurence are quite at variance with those published by Sievert (who quotes Kohlrausch). Quimby obtained the platinum-equivalent thicknesses without determining the values of the absorption coefficients. The experimental set-up employed by Quimby approximates the conditions under which radium is often used in therapy. Therefore the platinum-equivalent factors in Table II were calculated from Quimby's data. These factors are sufficiently accurate for radium therapy provided not more than 2 mm. of filter are used.

The tissue factors cannot be determined accurately by any simple formula. The increase of radiation due to scatter invalidates the use of the tissue absorption coefficients determined by Kohlrausch and Failla. Sievert included the tissue absorption coefficient in his calculation of dose from point and linear sources, but, in so doing, omitted the contribution from scattered radiation. The amount of scattered radiation depends upon the total

volume and character of the tissue irradiated. It cannot be calculated by any simple method and must therefore be measured. Such measurements were made by Laurence for various thicknesses of tissue. The tissue factors in Table III were obtained from Laurence's data by averaging the various values given for each thickness of tissue. At best, they must be considered rough approximations.

Finally, the measurement of distances in tissue cannot be made with precision because of practical difficulties. An error of 10 per cent in a distance measurement may

TABLE V

DIFFERENCE BETWEEN CONVERSION FACTORS CALCULATED WITH $\mu = 1.5 \text{ cm.}^{-1}$ AND THOSE CALCULATED WITH OTHER VALUES OF PLATINUM ABSORPTION COEFFICIENT

Thickness of Platinum Filter	Percentage Difference	
	$\mu = 2.0 \text{ cm.}^{-1}$	$\mu = 1.39 \text{ cm.}^{-1}$
0.0 mm.	+3%	0
0.5 mm.	0	0
1.0 mm.	-2%	+1%
1.5 mm.	-4%	+1%
2.0 mm.	-7%	+2%

mean an error of about 20 per cent in the dose calculation.

From this discussion, it is obvious that the calculation of dose in radium therapy is limited in accuracy by inherent and practical difficulties which require consideration in the evaluation of the final result.

The following examples illustrate a few of the applications of the point and linear source formulas.

Example 1. If a single capsule of radium, with a primary filter of 1.0 mm. of platinum, a secondary filter of 2.0 mm. of brass, and an active length of 1.6 cm., is placed in a cervical stump for 3,000 mg-hr., the dose delivered to the obturator node, estimated at 5.0 cm. from the cervical canal, may be calculated as follows:

The point source formula may be employed

since the distance is more than three times the active length of the source.

Platinum-equivalent factor for brass = 0.25
Equivalent filtration of 2.0 mm. brass
= $2 \times 0.25 = 0.5$ mm. Pt

Total filtration = $1.0 + 0.5 = 1.5$ mm. Pt

Conversion factor for 1.5 mm. Pt = 7.2

Distance = 5 cm.

Tissue factor for 5 cm. = 0.92

Therefore,

$$D = \frac{M \times I \times C \times S}{h^2} = \frac{3000 \times 7.2 \times 0.92}{5^2} = 795 \text{ r}_r.$$

Example 2. A linear source consists of three 15 mg. capsules of radium in a rubber tandem. The primary filter is 1.0 mm. of platinum. The over-all active length measures 6.0 cm. The time of application is 100 hours. The doses at various points in a line 3 cm. from the linear source and parallel to it may be calculated as follows:

A. At a point in the midplane (point \mathcal{Q}_1 , Fig. 5)

$$M = 45 \quad L = 6.0 \quad S \text{ (for 3 cm.)} = 0.94$$

$$t = 100 \quad h = 3.0$$

$$a = \frac{L}{2} = 3 \quad \frac{a}{h} = 1 \quad f(1) \text{ for 1.0 mm. Pt} = 5.98$$

$$L - a = 3 \quad \frac{L - a}{h} = 1 \quad f(1) \text{ for 1.0 mm. Pt} = 5.98$$

$$D = \frac{M \times t}{L \times h} \times \left[f\left(\frac{L - a}{h}\right) + f\left(\frac{a}{h}\right) \right] \times S$$

$$= \frac{45 \times 100}{6 \times 3} \times [5.98 + 5.98] \times 0.94$$

$$= 2800 \text{ r}_r$$

(For this problem, the ratio factors are equivalent to $2f(L/2h)$)

B. At a point 1.0 cm. from one end of the linear source (point \mathcal{Q}_2 , Fig. 5)

$$a = 1.0 \quad \frac{a}{h} = 0.33 \quad f(0.33) \text{ for 1.0 mm. Pt} = 2.48$$

$$L - a = 5.0 \quad \frac{L - a}{h} = 1.67 \quad f(1.67) \text{ for 1.0 mm. Pt} = 7.70$$

$$D = \frac{45 \times 100}{6 \times 3} \times [7.70 + 2.48] \times 0.94$$

$$= 2390 \text{ r}_r$$

C. At a point in the end plane (point \mathcal{Q}_3 , Fig. 5)

$$a = 0 \quad \frac{a}{h} = 0 \quad f(0) = 0$$

$$L - a = 6 \quad \frac{L - a}{h} = 2 \quad f(2) \text{ for 1.0 mm. Pt} = 8.21$$

$$D = \frac{45 \times 100}{6 \times 3} \times 8.21 \times 0.94$$

$$= 1930 \text{ r}_r$$

D. At a point 1.5 cm. beyond the end of the linear source (point \mathcal{Q}_4 , Fig. 5)

$$a = -1.5 \quad \frac{a}{h} = -0.5 \quad f(-0.5) \text{ for 1.0 mm. Pt} = -3.56$$

$$L - a = 7.5 \quad \frac{L - a}{h} = 2.5 \quad f(2.5) \text{ for 1.0 mm. Pt} = 8.72$$

$$D = \frac{45 \times 100}{6 \times 3} \times [8.72 - 3.56] \times 0.94$$

$$= 1210 \text{ r}_r$$

Example 3. The relative doses at the various points described in Example 2 may be estimated from the ratio factors, the midplane dose being taken as 100 per cent.

$$D \text{ at point } \mathcal{Q}_1 = 100\%$$

$$D \text{ at point } \mathcal{Q}_2 = \frac{7.70 + 2.48}{2 \times 5.98} \times 100$$

$$= 85.1\% \text{ of } D \text{ at point } \mathcal{Q}_1$$

$$D \text{ at point } \mathcal{Q}_3 = \frac{8.21}{2 \times 5.98} \times 100$$

$$= 68.6\% \text{ of } D \text{ at point } \mathcal{Q}_1$$

$$D \text{ at point } \mathcal{Q}_4 = \frac{8.72 - 3.56}{2 \times 5.98} \times 100$$

$$= 43.1\% \text{ of } D \text{ at point } \mathcal{Q}_1$$

These percentages check exactly with the actual doses obtained in Example 2.

Example 4. The number of milligram-hours of radium required to deliver 700 gamma roentgens to a point 5.0 cm. from the midpoint of the tandem used in the previous examples may be calculated as follows.

$$L=6.0 \quad h=5.0 \quad S=0.92$$

$$a=\frac{L}{2} \therefore \text{ratio factors} = 2f\left(\frac{L}{2h}\right)$$

$$\frac{L}{2h}=0.6 \quad f(0.6) \text{ for } 1.0 \text{ mm. Pt}=4.15$$

$$D=700$$

$$700=\frac{M \times t}{6 \times 5} \times 2 \times 4.15 \times 0.92$$

$$\therefore M \times t = 2750 \text{ mg-hr.}$$

SUMMARY

The following formulas have been derived for the calculation of dose from point and linear sources of radium in terms of the gamma roentgen:

1. The point source formula

$$D=\frac{M \times t \times C \times S}{h^2}$$

2. The linear source formula

$$D=\frac{M \times t}{L \times h} \times \left[f\left(\frac{L-a}{h}\right) + f\left(\frac{a}{h}\right) \right] \times S$$

A few useful simplifications of these formulas have also been derived.

The various factors concerned are given in the form of tables.

The significance of the various factors is discussed.

The limitations of accuracy of the formulas were analyzed.

Several examples were given to illustrate the application of the formulas.

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I wish to express my appreciation to Mr. Carl B. Braestrup and Dr. Sergei Feitelberg, physicists, Mount Sinai Hospital, for their helpful criticism and for their assistance with the mathematics and physics in this article.

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Twenty-eighth Annual Meeting: 1946, to be announced.

EDITORIAL

TUMORS AND TUMOR METASTASES IN THEIR RELATION TO TRAUMA

OUR advances in knowledge are a great stimulus to a revision of various subjects in medicine which have previously been accepted as established facts, and in no field of so-called established knowledge has this fact been more evidenced than in a re-assessment of mechanical trauma in its relation to bone tumors or bone metastases. Ewing,¹ several years ago, pointed out that "many recent fundamental contributions on the causation of tumors have an important bearing on the relation of trauma to cancer. When nothing definite was known about the effective exciting factors in mammary cancer it was permissible to adopt the traumatic theory in cases in which the clinical evidence pointed strongly that way." With our recent advancement in the experimental production of mammary cancer, particularly in mice, the traumatic origin becomes much less tenable. It is possible to produce cancer experimentally with many agents but always under specific conditions that are not related to trauma, and the experimental data reveal that the genesis of cancer requires quite peculiar factors which have not been found in the results of trauma, and the accumulation of knowledge thus gained has modified our views concerning cancers and their possible relation to simple traumas.

Quite recently, Saphir, Appel and Levinthal² have made an experimental attempt to localize tumor metastases in long bones

by mechanical trauma. They state that there are many references containing discussions dealing with the influence of trauma on tumor development, and numerous reports indicating that in some unexplained manner trauma may be a significant factor in initiating malignant growth, but that there are relatively few articles concerning the influence of trauma on the localization of metastases. Their experiments were carried on with this idea in mind. They were stimulated in their experimental researches by the conflicting evidence of relation of trauma to metastases and because of the importance of this problem from the medicolegal standpoint.

Their particular experimental study was undertaken "to ascertain whether or not trauma applied to long bones might be influential in the localization of metastases from a transplanted malignant tumor." In their experiments the Brown-Pearce rabbit tumor was used, for obvious reasons, namely that it is a highly malignant tumor, readily transplanted into the testes, from which it metastasizes early. In their experiment attempts were made to localize the metastases in long bones by a single mechanical trauma and also by chronic irritation. In their experimental animals bone metastases have not been observed in their stock tumor rabbits except in the spinal column, and then but rarely. When, however, they transplanted fragments of the Brown-Pearce carcinoma into the long bones (the femur) directly, the tumor grew well within the marrow spaces in all cases, soon invaded the periosteum and adjacent muscles, and metastasized extensively.

In a number of rabbits the left humerus was fractured and immediately afterwards

¹ Ewing, J. Modern attitude toward traumatic cancer. *Arch. Path.*, 1935, 19, 695-728.

² Saphir, O., Appel, M., and Levinthal, D. H. Attempts to localize tumor metastases in long bones by mechanical trauma. *Cancer Research*, 1945, 5, 722-723.

³ Jones, F. S., and Rous, P. On the cause of the localization of secondary tumors at points of injury. *J. Exper. Med.*, 1914, 29, 424-442.

an intravenous injection of a suspension of tumor cells was made into the ear vein. These rabbits were followed both clinically and roentgenographically. Roentgenograms of the entire skeleton of each rabbit were made after death. In those animals, at autopsy, which had received the intravenous transplantation, most of the metastases were found in the lungs, but the kidneys and liver were also involved. The region of the experimental fracture was carefully examined by means of roentgenograms in the gross, and a number of block sections were taken from the region of the fracture and the adjacent bone and soft tissue. There was no macroscopic evidence of tumor in this location. The histological examination revealed tremendous cellular proliferation in the region of the fracture and callus formation, which varied according to the interval between the time of fracture and the death of the animal. In several cases serial sections were cut from the region of the fracture but in none of these cases was there evidence of tumor cells at the site of the fracture.

To see what part chronic mechanical irritation might possibly play in the localization of tumor metastases, they introduced a piece of a small vitallium screw immediately beneath the periosteum in close contact with the cortex of the distal end of the femur. This screw was held in place by silk sutures and was placed so that with each movement of the leg the metal rubbed against the bone. In all of their experimental animals the position of this screw was verified by roentgenograms. Upon the death of the animals the position of the screw was studied again by means of roentgenograms to be sure that it had remained in place. A thickened periosteum, evidence of mechanical irritation, was almost invariably noted, and again wide-

spread metastases were recorded, but no gross evidence of tumor was encountered in any of the animals at any point of the mechanical irritation. Multiple sections taken from the bone in the area of the mechanical irritation and examined histologically revealed no evidence of tumor cells.

From these experiments the investigators concluded that mechanical trauma or chronic irritation of bones played no rôle in the localization of metastases from transplanted Brown-Pearce carcinomas in rabbits.

While it is not always easy to transfer animal experiments to the human, it is at least significant that the experimental data presented by Saphir and his associates quite closely agree with the ideas of many other observers, particularly Ewing, who has cautioned us that "Opinions regarding the possible traumatic origin of any tumor must be based on a full consideration of the location, known conditions of origin, structural peculiarities and clinical course of the tumor in each organ," that further generalizations may be invalid or misleading, that the interpretation of compensation laws should recognize that trauma is never the sole cause of cancer and is often only a subordinate, although determining cause, that the probability of coincidence is great, that aggravation by injury is rare and difficult to establish, and he emphasizes the fact that there is urgent need of more competent detailed analysis of individual cases of tumors that are possibly traumatic.

The experimental work of Saphir and his associates lends great weight to Ewing's discussion and it is such experimental work coupled with clinical observations that will in all probability lead us to a proper perspective regarding trauma and its relation to cancer or tumor formation.



SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

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ARKANSAS RADIOLOGICAL SOCIETY

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RADIOLOGICAL SOCIETY OF NORTH AMERICA

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BUFFALO RADIOLOGICAL SOCIETY

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CHICAGO ROENTGEN SOCIETY

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DETROIT ROENTGEN RAY AND RADIUM SOCIETY

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NORTH CAROLINA ROENTGEN RAY SOCIETY

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* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

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Medical Members' meeting held monthly on third Friday at 2:30 P.M. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)

Meets on the third Friday of each month at 4:45 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

FACULTY OF RADIOLOGISTS

Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

SECTION OF RADIOLOGY AND MEDICAL ELECTRICITY, AUSTRALASIAN MEDICAL CONGRESS

Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

RADIOLOGICAL SECTION OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION

Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

CANADIAN ASSOCIATION OF RADIOLOGISTS

Secretary, Dr. J. W. McKay, 1620 Cedar Ave., Montreal, P. Q.

SOCIÉTÉ CANADIENNE-FRANCAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES

Secretary, Dr. Origène Dufresne, 4120 Ontario St., East Montreal, P. Q.

SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION

Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MEDICAL ASSOCIATION

Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

SOUTH AMERICA

SOCIEDAD ARGENTINA DE RADIOLOGIA

Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

SOCIEDAD PERUANA DE RADIOLOGIA

Secretary, Dr. Victor Giannoni, Apartado, 2306, Lima, Peru. Meetings held monthly except during January, February and March, at the Asociación Médica Peruana "Daniel A. Carrión, Villalta, 218, Lima.

CONTINENTAL EUROPE

SOCIEDAD ESPAÑOLA DE RADIOLOGIA Y ELECTROLOGIA

Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

SOCIÉTÉ SUISSE DE RADIOLOGIE (SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT)

Secretary for French language, Dr. Babaianz, Geneva. *Secretary* for German language, Dr. Max Hopf, Effingerstrasse 49, Bern. Meets annually in different cities.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE

Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30. S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD:

USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.

Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

LENINGRAD ROENTGEN RAY SOCIETY

Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

MOSCOW ROENTGEN RAY SOCIETY

Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

SCANDINAVIAN ROENTGEN SOCIETIES

The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

SECOND INTER-AMERICAN CONGRESS OF RADIOLOGY

A letter just received from Dr. Pedro L. Fariñas, President of the Second Inter-American Congress of Radiology to be held in Havana, Cuba, November 17-22, 1946, states that he would like to have as soon as possible the names of the authors and titles of the papers which will be contributed from the United States. There is room for a limited number of papers on the program and it is suggested that all members of the American Roentgen Ray Society who expect to attend this Congress next November and who wish to present a paper, communicate *at once* with the undersigned, so that titles of papers may be sent to the central committee at Havana. Because of the long distances involved and the time consumed for transmission of the mails, it is necessary to issue the printed program much earlier than would ordinarily be the case, and a tentative program must be printed in the very near future.

It is therefore requested that all who plan to attend the Congress and give a paper or all who plan to make a contribution to the scientific exhibit, communicate with the undersigned at the earliest possible date.

JAMES T. CASE, M.D., Chairman
General Committee for the United States
20 North Wacker Drive
Chicago 6, Illinois

SECOND INTER-AMERICAN CONGRESS OF RADIOLOGY

NOVEMBER 17-22, 1946

Hotel Nacional, Habana, Cuba

PROGRAM OF THE SCIENTIFIC MEETINGS AND SOCIAL EVENTS

SUNDAY—NOVEMBER 17, 1946

From 2 to 6 P.M. Registration at the Headquarters of the Congress at the National Hotel, first floor.

GENERAL ASSEMBLY

- 9:00 P.M. Silver Room. The Honorable Dr. Ramón Grau San Martín, President of the Republic of Cuba, will deliver the opening address.
- 9:30 P.M. The President of the past "First Congress of Radiology," Dr. José F. Merlo Gómez, from Argentina, will proceed to turn over the Presidency to the President-elect of the "Second Inter-American Congress of Radiology," Dr. Pedro L. Fariñas, from Havana.
- 10:00 P.M. Presentation to the Audience of the Official Delegates.
- 11:00 P.M. Address "Radiology in America," by Dr. James T. Case.
- 12:00 M. Buffet.

MONDAY—NOVEMBER 18, 1946

- 9:00 A.M. Presentation of papers. There will be *six* papers. The maximum time allotted for each presentation is 20 minutes.
- 12:00 M. Reception at City Hall by the Mayor of Havana. Group lunches will be given by Officers of the Congress.
- 9:00 P.M. Official Symposium on the Diagnosis of *Cancer of the stomach*. The opening paper of the symposium will be allotted 30 minutes. There will be three more papers on the same subject with 20 minutes for each one of them.

TUESDAY—NOVEMBER 19, 1946

- 9:00 A.M. Presentation of papers. There will be *six* different papers. The maximum time allotted for each presentation is 20 minutes.
- 1:00 P.M. Lunch and typical Cuban Fiesta at one of the beach clubs.
- 4:00 P.M. Official symposium on the Diagnosis and Treatment of *Bone Tumors*. The opening papers of the symposium will be allotted 30 minutes. There will be three more papers on the same subject with 20 minutes' time for each one of them.
- 9:00 P.M. *Lecture*—Solemn session at the Hotel's Silver Room celebrating the

fiftieth anniversary of the discovery of X-Rays by Roentgen. The lecture will be delivered by the delegate of the Republic of Colombia.

WEDNESDAY—NOVEMBER 20, 1946

9:00 A.M. Presentation of papers. There will be *six* different papers. The maximum time allotted to each one of them is 20 minutes.

12:00 M. Lunch at the Country Club.

4:00 P.M. Official Symposium on Diagnosis and Treatment of *Bronchogenic carcinoma*.

The opening paper of the symposium will be allotted 30 minutes.

There will be three more papers on the same subject with 20 minutes' time for each one of them.

9:30 P.M. Concert by the Philharmonic Orchestra of Havana. Eric Kleiber conducting.

THURSDAY—NOVEMBER 21, 1946

9:00 A.M. Presentation of papers. There will be *six* different papers. The maximum time allotted for each presentation is 20 minutes.

1:00 P.M. Group lunches given by Officers of the Congress.

4:00 P.M. Official Symposium *Radiological mass survey*.

The opening paper of the symposium will be allotted 30 minutes.

There will be three more papers on the same subject with 20 minutes time for each one of them.

9:00 P.M. The Annual Banquet with entertainment and dancing at the National Casino.

FRIDAY—NOVEMBER 22, 1946

9:00 A.M. Presentation of papers. There will be six different papers. The maximum time allotted for each presentation is 20 minutes.

12:00 M. Visit to a Sugar Mill and typical country life entertainment, cock-fights, etc. Lunch in the country.

9:00 P.M. Council meeting for the Foundation

of the *Inter-American College of Radiology*.

Executive and Business sessions.

Elections.

SATURDAY—NOVEMBER 23, 1946

Free morning to visit the city and its surroundings.

3:00 P.M. Visit to Oriental Park. Race Track where Radiological handicap will be run.

Tea at the Jockey Club.

NOTES ON THE PROGRAM

The scientific program of the Second Inter-American Congress of Radiology will be closed the 31st July, 1946. Please be kind enough to send, before that date, the title of your paper with an abstract of the paper not exceeding one hundred words, which abstract will be published in the final program.

The program of the Scientific Exhibit will be closed on the 31st July. Send the title or your Exhibit and also a detailed description of the material. The x-ray films must be presented in reductions of 5×7 inches. Each film should carry its own description.

The Commercial Exhibit will display the best on modern equipment and x-ray accessories. We have rented space for the leading x-ray concerns.

Transportation facilities have been asked from and promised by Pan American Airways. You, as a Congressman, are entitled to a discount of 15% on your ticket over the usual 10% discount for round trip fare. Please write our Secretary as soon as possible confirming your decision to come, so we will be able to make reservations at the hotel.

The Congress fee is \$10.00 (U. S. dollars). You can either send the money directly to us or through your x-ray society, or also pay at our Registration Booth in Havana.

Members notifying their participation will be met at the airport by members and ladies of the Reception Committee. We will assist you in any formalities with the Immigration authorities and will take care of your arrival at the National Hotel.

It has been decided that all meetings and official social gatherings will be absolutely informal. Due to difficulties in transportation light luggage is suggested.

The climate in November in Cuba is so mild that nearly every day you can enjoy beach recreation. There is no need for an overcoat, bring your spring clothes, they are all right for our climate in winter. The ladies may bring light furs.

Besides the scientific and social events officially stipulated in the program, we have also organized several entertainment and cultural gatherings for

all to enjoy. All exclusive Clubs and Casinos will be open to Congressmen and their families.

Officials and ladies of the Social Committee will have the great pleasure of assisting anybody interested in visiting the historic monuments, churches, museums, clubs, beaches, government buildings, etc., or may have the intention of buying anything in our Department Stores.

Ladies will have their Registration desk next to the Registration Booth of the Congress on the first floor of the National Hotel.

Our traditional Cuban hospitality will not fail. You may be sure that your Havana winter days will be unforgettable.

CANCER TEACHING DAY

A Cancer Teaching Day will be held at the Hotel Jamestown, Jamestown, New York on Thursday, February 28, 1946. This is presented under the auspices of the Medical Society of the County of Chautauqua, Jamestown Medical Society, Medical Society of the State of New York, and the New York State Department of Health, Division of Cancer Control. The meeting will be called to order at 2:30 P.M., and the paper of the afternoon will be presented by Louis C. Kress, M.D., Director, State Institute for the Study of Malignant Diseases, Buffalo, New York, on "What the Public Should Know about Cancer."

Dinner will be served at the Hotel Jamestown at 6:30 P.M. Advance reservations are required.

The evening meeting will begin at 8 P.M. at which the following two papers will be presented: "Malignancies of the Uterus" by Clyde L. Randall, M.D., Professor of Gynecology, University of Buffalo School of Medicine, Buffalo, New York; "Cancer of the Breast" by Samuel J. Stabins, M.D., Assistant Professor of Surgery, University of Rochester School of Medicine and Dentistry, Rochester, New York.

MESSAGE FROM THE SOVIET UNION

The following cable was recently sent by the radiologists of the Soviet Union to American radiologists on the occasion of the fiftieth anniversary of the discovery of the roentgen ray. The message was trans-

mitted by the American Soviet Society to the Secretary of the American Roentgen Ray Society who in turn submitted it for publication in this JOURNAL:

On the occasion of the fiftieth anniversary of the discovery of the x-rays and radioactivities American roentgenology, on marking this momentous date this January, all Soviet roentgenologists and radiologists—numbering many thousands—warmly greet their overseas colleagues in the United States. Soviet biology highly appreciates great contribution made to treasury of world roentgenology and radiology by our American colleagues during the past half century. Soviet roentgenologists and radiologists have always closely followed notable achievements and progress of their American coworkers in this field. We sincerely wish our American friends every success in their further work.

PROFESSOR S. REINBERG
On Behalf Jubilee Committee

UROLOGY AWARD

The American Urological Association offers an annual award "not to exceed \$500" for an essay (or essays) on the result of some specific clinical or laboratory research in Urology. The amount of the prize is based on the merits of the work presented, and if the Committee on Scientific Research deem none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years. All interested should write the Secretary, for full particulars.

The selected essay (or essays) will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Netherland Plaza, Cincinnati, Ohio, July 22-25, 1946.

Essays must be in the hands of the Secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis 3, Tennessee, on or before July 1, 1946.

Committee on Scientific Research
JUDSON B. GILBERT
ANSON L. CLARK
MILEY B. WESSON, *Chairman*

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

NEURO-OPHTHALMOLOGY. By Donald J. Lyle, B.S., M.D., F.A.C.S., Lecturer on Neuro-Ophthalmology, Department of Anatomy, Medical College of the University of Cincinnati; Attending Ophthalmologist to the Good Samaritan Hospital, Christ Hospital, Jewish Hospital, St. Mary's Hospital and Children's Hospital. Cloth. Price, \$10.50. Pp. 398, with 529 illustrations. Springfield, Illinois: Charles C Thomas, 1945.

For years Dr. Lyle's exhibits in neuro-ophthalmology have adorned the scientific exhibit sections of medical conventions. Out of these exhibits, which have grown from year to year in scope and depth, has developed the book on Neuro-Ophthalmology which lies before us. In it the author has endeavored to bring together "in brief, but comprehensive and coordinated matter," the many phases of neurology that make up neuro-ophthalmology. The author's own background in neurology is dominantly an anatomical one which he acquired as a pupil of A. R. Vonderahe, at the University of Cincinnati. It is, therefore, not surprising that neuro-anatomy figures very prominently in Lyle's Neuro-Ophthalmology, with neurophysiology and theories of all kinds keeping well in the background.

Another characteristic of the book is the abundant factual material which is included in the form of 130 case histories and which makes for greater practicality, lucidity and vividness of the text. In 126 of these cases the diagnosis had been confirmed by the findings at operation or autopsy. Extensive use has been made of combined illustrations showing for instance, on the same page, the ophthalmoscopic picture and the perimetric, roentgenologic or autopsy findings. The ophthalmoscopic findings have been recorded in black and white, stereoptic or single photographs of the fundus. Because of the importance of color in ophthalmoscopic diagnosis, it is hoped that in future editions the black and white fundus photographs will be replaced with kodachrome pictures.

Aiming at comprehensiveness, the author has perhaps included more elementary ophthalmology than would have been necessary in a book

of this kind. His first chapter, for instance, entitled, "Embryological Development of the Neural Structure of the Eye," while it represents a logical starting point for the book, contains chiefly fundamental ophthalmology. Outstanding chapters, from the standpoint of the ophthalmologist, are the ones dealing with the arterial vascular system of the brain and the presentation of the cerebrospinal fluid system. The selection of neurological material has been made judiciously, so that the ophthalmologist will find in the book the information necessary for the understanding of practically all the neurological diseases that he is likely to encounter. A bibliography containing over 1700 references and covering the last eight years is included.

In summary, Dr. Lyle's Neuro-Ophthalmology is intended to guide the ophthalmologist in all neurological matters. There is no doubt in the reviewer's mind that the book will serve well in that capacity.

PETER C. KRONFELD

ESCLERÓSES VALVULARES CALCIFICADAS: ESTUDO ANÁTOMO-PATOLÓGICO, RADIOLÓGICO E CLÍNICO, COM APRESENTAÇÃO DE CEM CASOS. By Dr. Roberto Menezes de Oliveria, Capitão Médico do Corpo de Saúde da Aeronáutica, Diplomado em Medicina de Aviação pela Diretoria de Aeronáutica do Ministério da Marinha, etc. Paper. Pp. 155, with 67 illustrations. Rio de Janeiro, Brasil: Tipografia do Patromato, 1943.

This monograph, carefully edited and well printed on high quality paper, is a worthwhile work. The author's analysis of the result of his investigation of one hundred cases of valvular calcification, encountered at the Peter Bent Brigham Hospital, in Boston, is well presented and each statement is based on abundant clinical, roentgenologic, pathologic and statistical proof. The relatively voluminous reports of cases are illustrated by about fifty well reproduced roentgenograms. In the text, the author mentions more than one hundred bibliographic references.

The author warns against the usually incom-

plete diagnoses in the field of his investigation. Concerning twenty-five of the cases of calcified annulus fibrosus, data derived from necropsy are given. Certain of the author's findings from this source and from his clinical studies are of particular interest. A purely degenerative process limited to the valve rings does not interfere with function whereas a process which results in calcification indicates a lesion of the valve. Calcified lesions of the aortic valvular region involve both ring and valves. The presence of calcification of the mitral valve is pathognomonic of mitral stenosis only when limited to the valve proper. Calcification of the annulus fibrosus of the mitral valve is one of the most frequent and earliest signs of arteriosclerosis. In rheumatic cases any calcification which extends to the valves proper indicates a functional valvular lesion. The degenerative signs found with cardiac degeneration associated with calcification include: coronary calcification (25 per cent); calcification of the aorta (20 per cent); hypertrophic changes in the vertebrae; cholelithiasis; hyperostosis of the skull; osteoporosis and Paget's disease, and kyphosis. Disturbance in calcium metabolism was present in 20 per cent of the cases. Predominance of the condition among females is explicable through the disturbance of calcium metabolism after menopause and the higher incidence of hypertension among women.

The six pages of methodically presented summary and conclusions are an invaluable part of the work. Besides being printed in the author's native Portuguese they also appear translated into English. The author concludes that roentgenologic studies of valvular calcification facilitate investigation of the following: (1) exact movements of cardiac valves; (2) movements associated with suction exerted by the base of the heart; (3) the importance of this latter movement in the determination of cardiac output, and (4) the fallacy of measuring cardiac output by registering the difference between systolic and diastolic siliouettes.

Great credit is due the author for the thorough manner in which he has handled his subject. This work should inspire further contributions on roentgenology of the heart, especially from Latin America.

SEBASTIÃO V. FRANCO

A BIBLIOGRAPHY OF AVIATION MEDICINE: SUPPLEMENT. By Phebe Margaret Hoff, Ebbe Curtis Hoff and John Farquhar Fulton.

Cloth. Price, \$2.50. Pp. 109. Published (1944) by the Committee on Aviation Medicine, Division of Medical Sciences, National Research Council, Acting for the Committee on Medical Research, Office of Scientific Research and Development, Washington, D. C. Distributed by Charles C Thomas, Springfield, Illinois.

This supplement is a continuation of the previous original Bibliography of Aviation Medicine compiled by Hoff and Fulton, and published in 1942. The present volume is made up of a list of 2,336 entries; these, with the references in the first volume, comprise a total of over 7,000 items devoted to this special field.

Despite the timely, and in fact imperative, interest in all matters pertaining to the aviator on account of war conditions, one would hardly believe that so many articles dealing with this subject could be published in such a relatively short time. An inspection of the volume, however, reveals at once how far reaching this field is and how many other interests are closely associated with aviation, especially in war time. For example, there is an added topic in this supplementary volume which deals with Survival and Rescue. References are found in this section which are concerned with such pertinent subjects as the effects of sea water on experimental animals, shark bite, points of interest in Navy fishing instructions, the effect of exposure on flyers to Arctic waters, etc., etc. The remarkable and dramatic story of the development of the Air Transport of the Sick and Wounded has been continued in the supplement by the addition of new references since the first publication in 1942.

In order that the reader may obtain some idea of the extent and nature of the bibliography, it should be stated that the material is divided into fourteen main topics, as follows: (1) History and General Aspects of Aviation Medicine, (2) The Special Physiology of Aviation and Conditions Simulating Flight, (3) The Special Pharmacology of Aviation and Conditions Simulating Flight, (4) The Special Psychology of Aviation and Conditions Simulating Flight, (5) Aeromicrobiology (Bacteriology and Immunology in Aviation and High Altitudes), (6) Diseases and Accidents in Aviation and Conditions Simulating Flight, (7) Selection and Assessment of Efficiency of Flight Personnel, (8) Training, Performance and Fatigue of

Flight Personnel, (9) Protection of Flight Personnel, Preventive Medicine and Therapeutics of Aviation, (10) Aviation and Public Health (Sanitary Aviation), (11) Organization of Aviation Medicine, (12) Special Problems, (13) General Studies in Aviation Medicine, and (14) Bibliographies.

This publication commands interest for several reasons: first, because it is a collection of bibliographical information about a new and special topic which is of immediate importance and growing interest; second, because it appears to be a model pattern for the presentation of medical bibliography; and third, because the publication is obviously more than a simple and accurate compilation of data. As the authors say, a classified bibliography to deserve its name, must preserve an "analytical function, else it becomes merely a sterile list of references." The reviewer is impressed with the care, the thought and the planning which have obviously been devoted to the selection, classification and arrangement of the material in this volume. It is to be hoped that other such carefully prepared bibliographies relating to medical topics will be available in the future. The collection and preparation of such data are not, however, a routine task to which the novice should be assigned for such work demands the mature and intelligent judgment of one experienced in the field. Any one who contemplates the preparation of such a collection would do well to peruse the work of Hoff, Hoff and Fulton and use it as an effective method of presentation.

C. C. STURGIS

BOOKS RECEIVED

PEDIATRIC X-RAY DIAGNOSIS: A TEXTBOOK FOR STUDENTS AND PRACTITIONERS OF PEDIATRICS, SURGERY & RADIOLOGY. By John Caffey, A.B., M.D., Associate Professor of Pediatrics, College of Physicians and Surgeons, Columbia University; Associate Pediatrician and Roentgenologist, Babies Hospital and Vanderbilt Clinic, New York City, etc. Cloth. Price, \$12.50. Pp. 838, with 711 illustrations. Chicago: Year Book Publishers, 1945.

NUTRITION AND CHEMICAL GROWTH IN CHILDHOOD. Volume II. Original Data. By Icie G. Macy, Ph.D., Sc.D., Director of the Research Laboratory, Children's Fund of Michigan. With a Foreword by Lawrence Reynolds, M.D., Editor of the *AMERICAN*

JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY. And a Supplement by Julia O. Holmes, Ph.D. Cloth. Price, \$10.00. Pp. 1027 (433-1460), with 706 illustrations. Springfield, Illinois: Charles C Thomas, 1946.

WHOOPING COUGH. By Joseph H. Lapin, B. Chem., M.D., Adjunct Pediatrician, Bronx Hospital; Associate in Contagion, Riverside Hospital for Contagious Diseases, New York. Cloth. Price, \$4.50. Pp. 238, with 40 illustrations. Springfield, Illinois: Charles C Thomas, 1943.

PULMONARY TUBERCULOSIS IN THE ADULT: ITS FUNDAMENTAL ASPECTS. By Max Pinner, M.D., Chief, Division of Pulmonary Diseases, Montefiore Hospital for Chronic Diseases, New York; Editor, *American Review of Tuberculosis*; Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, \$7.50. Pp. 579, with 59 illustrations. Springfield, Illinois: Charles C Thomas, 1945.

THE DENTAL TREATMENT OF MAXILLO-FACIAL INJURIES: WITH SUPPLEMENTARY MATERIAL ON CASES AND TECHNIQUES. By W. Kelsey Fry, M.C., M.R.C.S., L.R.C.P., L.D.S., R.C.S. (Eng.), Consulting Dental Surgeon to the Royal Air Force; Consulting Dental Surgeon to the Ministry of Health; Dental Surgeon to Guy's Hospital; P. Rae Shepherd, L.D.S., R.C.S. (Eng.), Dental Surgeon, East Grinstead Maxillo-facial Unit; Alan C. McLeod, D.D.S (Penn.), B.Sc. (Dent.), Toronto, L.D.S., R.C.S. (Eng.), Dental Surgeon, East Grinstead Maxillo-facial Unit; and Gilbert J. Parfitt, M.R.C.S., L.R.C.P., L.D.S., R.C.S. (Eng.), Dental Surgeon, East Grinstead Maxillo-facial Unit. With Foreword by Professor F. R. Fraser, M.D., F.R.C.P., Director General, Emergency Medical Service; and a Section on Fractures of the Middle Third of the Face by A. H. McIndoe, M.S., F.R.C.S., F.A.C.S., Consulting Plastic Surgeon to the Royal Air Force, Surgeon-in-Charge, East Grinstead Maxillo-facial Unit. Cloth. Price, \$6.50. Pp. 434, with many illustrations. Philadelphia: J. B. Lippincott Company, 1944.

THE NEUROSURGICAL PATIENT: HIS PROBLEMS OF DIAGNOSIS AND CARE. By Carl W. Rand. Clinical Professor of Neurological Surgery, University of Southern California, School of Medicine, Los Angeles, California. Cloth. Price, \$4.00. Pp. 576, with 121 illustrations. Springfield, Illinois: Charles C Thomas, 1944.

- AN ATLAS OF ANATOMY. By J. C. Boileau Grant, M.C., M.B., Ch.B., F.R.C.S. (Edin.), Professor of Anatomy in the University of Toronto. In two volumes. Volume II. Vertebrae and Vertebral Column, Thorax, Head and Neck. Cloth. Price, \$5.00. Pp. 390, with 460 illustrations. Baltimore, Maryland: Williams and Wilkins Company, 1943.
- DR. W. C. RÖNTGEN. By Otto Glasser, Cleveland Clinic Foundation. Cloth. Price, \$4.50. Pp. 169, with illustrations. Springfield, Illinois: Charles C Thomas, 1945.
- FRANÇOIS MAGENDIE: PIONEER IN EXPERIMENTAL PHYSIOLOGY AND SCIENTIFIC MEDICINE IN XIX CENTURY FRANCE. By J. M. D. Olmsted, Professor of Physiology, University of California. Cloth. Price, \$5.00. Pp. 290, with illustrations. New York: Schuman's, 1944.
- A BIO-BIBLIOGRAPHY OF ANDREAS VESALIUS. By Harvey Cushing. Cloth. Price, \$15.00. Pp. 229, with many illustrations. New York: Schuman's, 1943.
- THE HARVEY CUSHING COLLECTION OF BOOKS AND MANUSCRIPTS. Cloth. Price, \$8.50. Pp. 207. New York: Schuman's, 1943.
- RADIUMDOSIMETRIE. Von Dr. phil. Walter Minder, Technischer Leiter des Institutes der Bernischen Radiumstiftung in Bern. Cloth. Price, \$5.50. Pp. 183, with 97 illustrations. Wien: Julius Springer, 1941. J. W. Edwards, Publisher, Ann Arbor, Michigan.
- SIEBZEHN JAHRE STRAHLENTHERAPIE DER KREBSE. Zürcher Erfahrungen 1919-1935. Von Hans R. Schinz und Adolf Zuppinger. Cloth. Price, \$11.75. Pp. 340, with 95 illustrations and 213 tables. Leipzig: Georg Thieme, 1937. J. W. Edwards, Publisher, Ann Arbor, Michigan. (This book has already been reviewed in the AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY, 1938, 40, 778.)
- KURZWELLENTHERAPIE. Von Dr. Josef Kowarschik, Professor für physikalische Therapie an der Universität Wien. Third edition. Cloth. Price, \$4.25. Pp. 143, with 138 illustrations. Wien: Springer, 1943. J. W. Edwards, Publisher, Ann Arbor, Michigan.
- RÖNTGENPHYSIK. Von Dr. med. Adolf Liechti, Professor für medizinische Radiologie; Direktor des Röntgeninstitutes der Universität Bern. Mit Beiträgen von Dr. phil. Walter Minder, Technischer Leiter des Institutes der Bernischen Radiumstiftung. Cloth. Price, \$11.75. Pp. 308, with 227 illustrations. Wien: Julius Springer, 1939. J. W. Edwards, Publisher, Ann Arbor, Michigan.
- ULTRAVIOLETTE STRAHLEN: IHRE ERZEUGUNG, MESSUNG UND ANWENDUNG IN MEDIZIN, BIOLOGIE UND TECHNIK. Von A. E. Herbert Meyer, Dr. phil., and Ernst Otto Seitz, Dr. phil. Mit einem Geleitwort von Professor Dr. B. Rajewsky, Direktor des Kaiser-Wilhelm-Institutes für Biophysik, Frankfurt a. M. Cloth. Price, \$10.00. Pp. 308, with 217 illustrations and 40 tables. Berlin: Walter de Gruyter & Co., 1942. J. W. Edwards, Publisher, Ann Arbor, Michigan.
- ULTRAKURZWELLEN IN IHREN MEDIZINISCH-BIOLOGISCHEN ANWENDUNGEN. Von H. Dänzer, H. E. Hollmann, B. Rajewsky, H. Schaefer and E. Schliephake. Cloth. Price, \$8.40. Pp. 308, with 188 illustrations and 24 tables. Leipzig: Georg Thieme, 1938. J. W. Edwards, Publisher, Ann Arbor, Michigan.
- INVISIBLE RADIATIONS OF ORGANISMS. By Otto Rahn, Professor of Bacteriology, Cornell University. With an Introduction to the Physics of Radiation. By Sidney W. Barnes, Research Associate in Physics, University of Rochester. (Protoplasma-Monographien, Volume 9.) Cloth. Price, \$4.75. Pp. 215, with 52 illustrations. Berlin: Gebrüder Borntraeger, 1936. J. W. Edwards, Publisher, Ann Arbor, Michigan.



DEPARTMENT OF TECHNIQUE

Department Editor: ROBERT B. TAFT, M.D., B.S., M.A., 103 Rutledge Ave.
Charleston, S. C.

A DEMONSTRATION ROENTGEN-RAY MACHINE "LIVE" CIRCUIT-DIAGRAM MODEL*

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NUMEROUS training aids have been devised for the study of roentgen machines and their electrical circuits. We are aware of demonstration types of roentgen machines used for these purposes. One of us has had the opportunity of using and becoming familiar with the training board used at the Army School of Roentgenology and the electric model of a roentgen machine constructed by Williams¹ and in use at the Mayo Foundation.

The demonstration apparatus used at the Army School of Roentgenology is of wall-display type and produces roentgen rays. The electric model in use at the Mayo Foundation is constructed from radio parts including radio rectifier tubes for demonstration of rectifying circuits, their resultant wave forms and their effect on the quantity and quality of the radiation produced. This model functions at low voltage and was constructed primarily to demonstrate basic principles of roentgen machines and common types of rectifying circuits.

Incorporating the methods of teaching already successfully used in Army Signal Corp Schools, we have designed a roentgen machine (Fig. 1 and 2) with a "live" diagram-circuit broken down into teaching units, divided as follows:

Autotransformer unit	(Fig. 1, No. 1—yellow)
High voltage transformer unit	(Fig. 1, No. 2—red)
Rectifier units	(Fig. 1, No. 3—blue)
Full-wave rectification unit (bridge rectifier)	(Fig. 1, No. 3A—blue)
Half-wave rectification unit	(Fig. 1, No. 3B—blue)
Self-rectification unit	(Fig. 1, No. 3C—blue)
Control circuit unit	(Fig. 1, No. 4—orange)
Filament circuit unit	(Fig. 1, No. 5—gray)
Roentgen tube unit	(Fig. 1, No. 6—green)
Oscilloscope	(Fig. 1, No. 7—separate unit)
Hand timer	(Fig. 1, No. 8—accessory)

Actual parts are shown on the panel and are all integral working parts of the "live" circuit except the "high tension" transformer, details of which will be mentioned later. Certain parts are included behind the panel and incorporated within the circuit behind the board to produce desired results as expected from the basic exterior demonstration diagram.

Our circuit is so designed that three machines can be demonstrated readily: full-wave rectifier with 100 ma., "100 kv." (peak) (Fig. 1, 3A); half-wave rectifier with 60 ma., "100 kv." (peak) (Fig. 1, 3B, Fig. 2, 3B); and self-rectifier 30 ma., "100 kv."

¹ Williams, M. M. D. Electric model of an x-ray machine. *Radiology*, 1942, 38, 338-349.

* Constructed at Central Signal Corps School, Camp Crowder, Missouri.

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(peak) (Fig. 1, 3c, Fig. 2, 3c). Within limits, these machines are operated much like an ordinary roentgen machine. As safety factors, production of actual high tension voltage and development of roentgen rays are eliminated as unnecessary.

Primary circuit voltages, kilovoltage, and milliamperage measurements are readily visualized in approximately correct meter readings. A gas-filled rectifier (tungar rec-

liamperage wave forms are studied. (We have used 3 inch and 7 inch oscilloscopes, the former for classroom demonstrations; the latter for larger groups.)

THE CIRCUIT

The design, in which a standard simplified circuit is broken down into six subdivisions, already enumerated, allows in panel 3 (Fig. 1) a substitution of the three

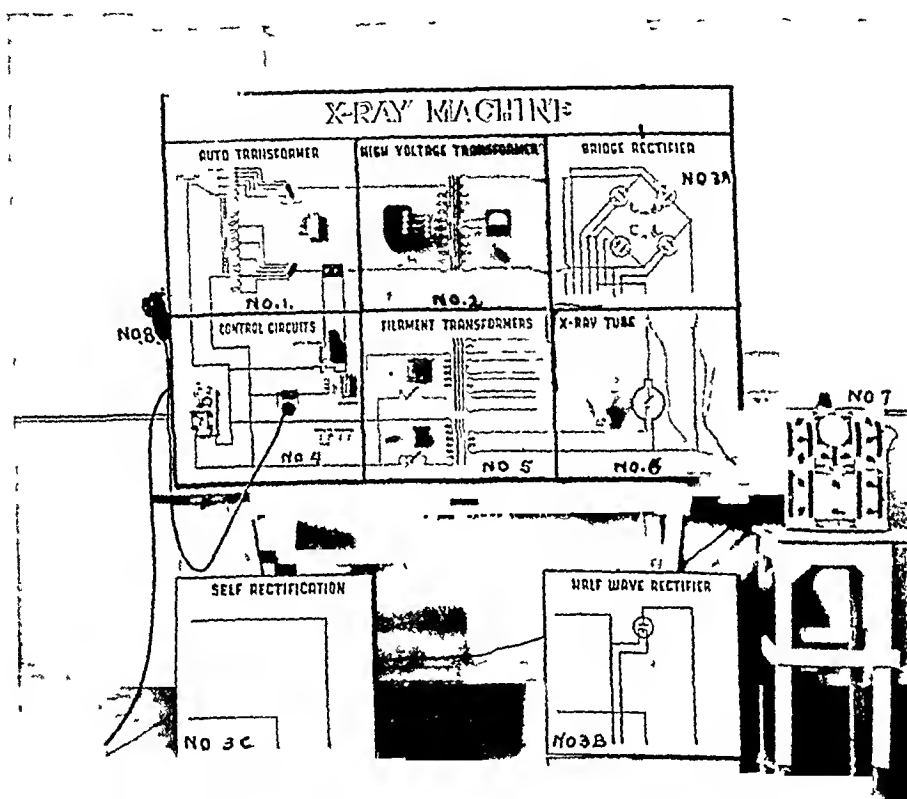


FIG. 1. Demonstration roentgen-ray machine. Full-wave rectification panel in circuit.

tifier with base removed) is chosen as the "roentgen tube" because rectified current is produced, filament changes result in visual proof of milliamperage change, the photoelectric effect of electron emission is demonstrable, and the tube is similar in appearance to a roentgen tube with cathode and anode visible (Fig. 1, No. 6).

Through the use of an oscilloscope (Fig. 1, No 7), voltage wave form, including rectification, is shown in various parts of the circuit. By connecting a 100 to 200 ohm resistor into the "high tension" circuit, mil-

types of rectification units without disturbing the remainder of the circuit. The other panels are thus kept in a fixed position.

The machine is constructed on a 6 by 4 ft. board mounted vertically and supported on a shelf 18 inches wide, the latter also serving as a counter for holding plug-in wires, resistors, and other associated training aids. Allowing for a 6 inch panel across the top for title, the board is divided into six units, plus two substitution units, each section measuring 21 by 24 inches. Panels

are painted a different color for better visualization of each unit. The circuit diagram is painted on the board in solid black lines as seen in Figure 1.

AUTOTRANSFORMER UNIT

The upper left hand panel (painted yellow) contains the autotransformer (Fig. 1, No. 1) hand wound, using the core of a

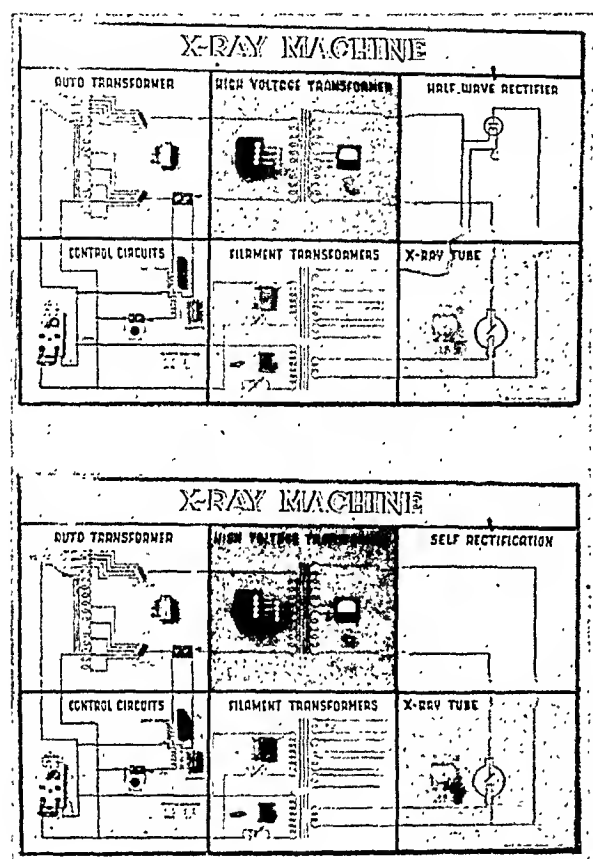


FIG. 2. Demonstration roentgen-ray machine showing half-wave rectification panel (A) and self-rectification (B) as part of circuit. (A, above; B below.)

small radio transformer. Taps are brought out to give secondary voltages ranging from 50 to 150 volts. Major tap controls allow for 20 volt gradations and minor tap controls for 5 volt changes. On the primary side of the autotransformer, line voltage compensation is effected through 100, 110, 120 and 130 volt taps.

The leads from the autotransformer (Fig. 3) are seen behind the board, with the fixed

primary lead connected to one side of the A.C. line coming from the control circuit unit. The four primary tap leads (line voltage compensation) connect to snap fasteners on the board. The other A.C. line lead is also brought to the front surface of the board and terminates in a snap to fit any one of the snap fasteners of the primary taps.

Secondary taps for the major adjustments are connected to a five-position wafer switch. Switch and leads are mounted behind the board with control knobs placed on the surface of board over the painted taps of the diagram. Minor control taps are similarly connected behind the board. The two leads from the common points on the wafer switches are connected to snap fasteners at the right edge of this panel, the lower also incorporating a knife switch for manual timing. The control unit can thus be excluded from the circuit.

By the method described, the painted diagram is incorporated into the circuit through live snap fastener taps which are available on the front side of the board. Each unit is similarly constructed in this regard.

HIGH VOLTAGE TRANSFORMER UNIT

The second panel (Fig. 1 and 2, No. 2) should normally include a functioning high tension transformer. The use of a training aid by inexperienced personnel (enlisted men and WAC trainees in our department) precluded the use of dangerous voltages. Therefore, this panel (painted red) shows the schematic diagram of a high voltage transformer. The transformer mounted on this section, however, is a "dummy" with the case made from the end of a pressed-meat can (painted black) and four stand-off insulators. Realism is obtained by running two "low voltage" (dummy) leads into the transformer case through rubber grommets and running four "high voltage" (dummy) secondary leads from the stand-off insulators to four similar high tension insulators on the display panel (see Fig. 1).

The meter (Fig. 4), also mounted on this

panel in the conventional manner, is shown grounded at zero potential in the secondary circuit. Through the use of a three-pole, three-position switch, the meter does triple duty, serving to record volts, "kilovolts" and milliamperes. As a millimeter (first position of switch—ma.) it is actually mounted directly in the circuit between the

simultaneously connects the leads from the knife switch (autotransformer panel) to the rectifier panel, thus restoring the circuit that is otherwise broken as the milliammeter is removed. The 2000 ohm resistance will permit a full scale deflection of 200 volts, the face of the meter being calibrated accordingly.

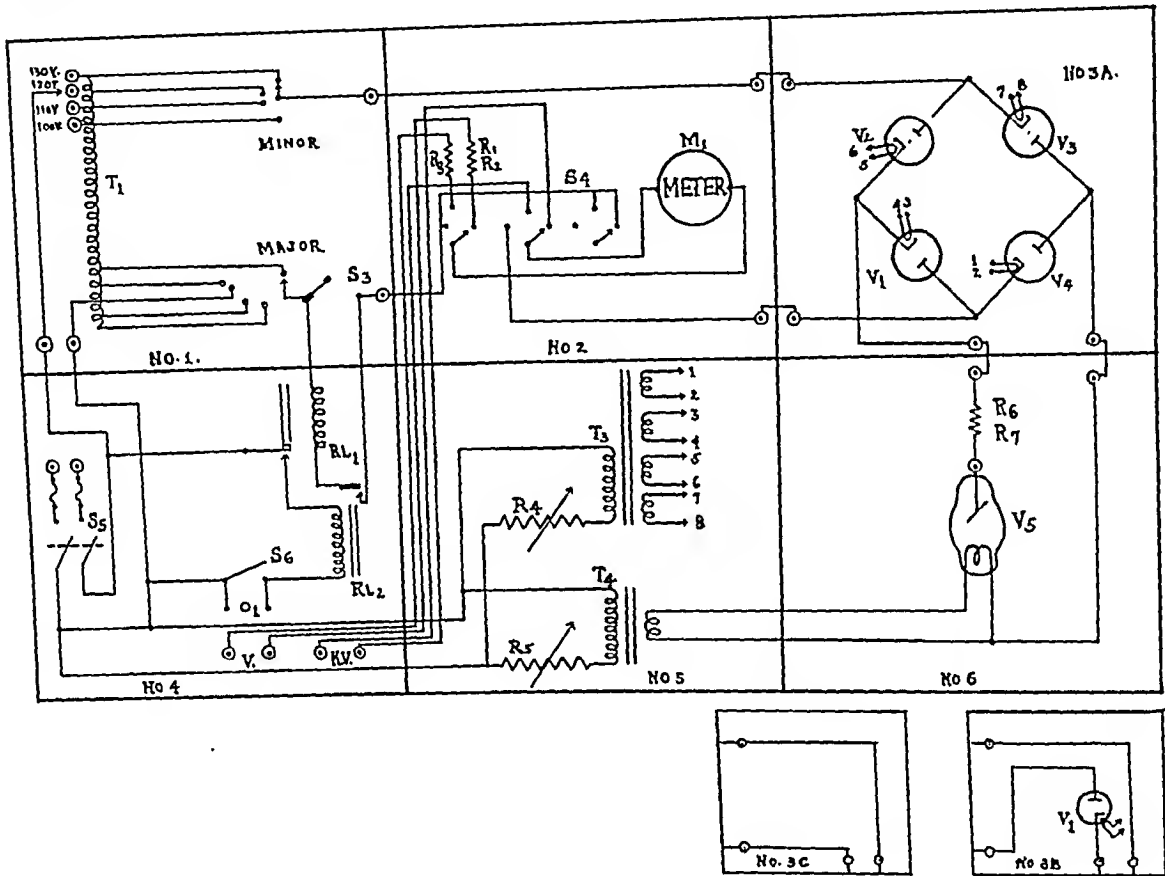


FIG. 3. Diagram of a circuit as actually found on back side of demonstration board with full-wave rectification panel (No. 3c) inserted. Substitution panels for half-wave rectification (No. 3b) are shown in smaller diagrams below. See Figure 4 for detail of all-purpose meter diagram (No. 2).

autotransformer and the rectifier (see Fig. 2) and is shunted (by an internal shunt) to read 100 ma. at full-scale deflection.

By turning the selector switch to the second position (volts) the meter is connected through a 2000 ohm resistor to the volts terminals on the control circuit panel (Fig. 1, No. 4) This outlet allows for its incorporation into the primary or control circuits for voltage measurements at any snap-faster connections. The selector switch

The third position of the selector switch ("kv.") connects the meter through a 1500 ohm resistance to the ("kv.") terminals on the control circuit panel. The 1500 ohm resistance will result in a full scale deflection of 150 volts but the face of the scale is not so calibrated. The maximum output of the autotransformer (with line voltage compensation taps correctly set) is 150 volts, and this voltage connected to the kilovolt terminals will give a full meter

scale deflection. If the machine had an actual high tension transformer, the high tension equivalent of 150 volts on the auto-transformer would be 100 kv. on the secondary circuit. Therefore, a meter scale 0-100 is used as the kilovolt scale. Thus, voltmeter leads taken from the high tension side of the high voltage transformer and connected to the kilovolt taps will read a fictitious peak of 100 kv. for 150 peak volts of primary and proportionately

rectly through from high voltage transformer to the roentgen tube. By replacing this panel with the *half-wave rectifier* panel (Fig. 1, No 3B) a circuit incorporating a single radio tube rectifier is made possible. By inserting a third panel (Fig. 1, No. 3A) a *full-wave rectifier* becomes an integral part of the circuit. This unit demonstrates the usual type of permanent installation seen. By removing one valve tube from this circuit, the oscilloscope also shows the

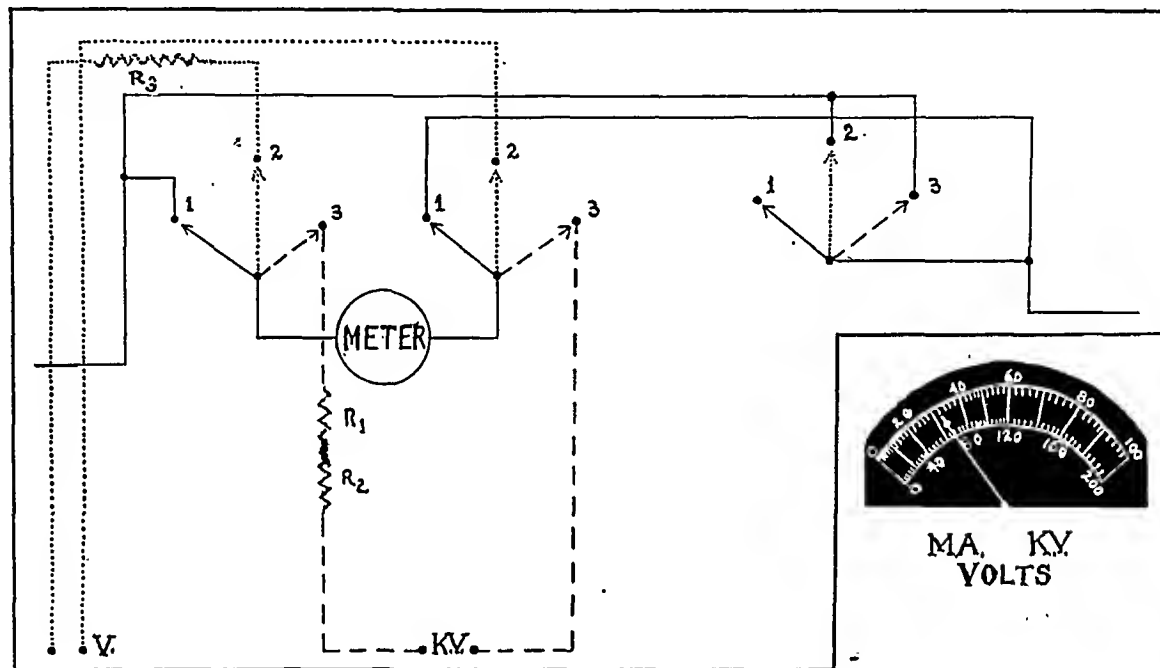


FIG. 4. Detailed diagram of circuit using an all-purpose meter (see insert) with a three-hole, three-position switch. Milliamperage is recorded with switch in position 1, voltage in position 2, and kilovoltage in position 3. Voltmeter and kilovoltmeter terminals are seen in control panel (Fig. 1 and 3, No. 4).

lesser "kilovolts" when tapped down through major and minor controls (secondary circuit of autotransformer).

RECTIFIER CIRCUIT UNITS

The third panel, painted blue (Fig. 1, No. 3, A, B or C), contains the rectifier circuit in which the versatility of the board is increased. As mentioned earlier, simple demonstration of various types of rectification is done by making interchangeable panels. The *self-rectification* panel (Fig. 1, No. 3c) is used for demonstration of the Army portable self-rectifying roentgen unit in its basic form. Wiring is carried di-

change from full-wave to half-wave rectification, which occurs with loss of one or both tubes which are paired in series in the full-wave (bridge) rectifying circuit.

CONTROL CIRCUIT UNIT

The *control circuit* (Fig. 1, No. 4), painted orange, contains the following essentials: main switch (double pole, single throw) and fuses connected to 110 volt A.C. outlet, contactor, circuit breaker, knife switch for manual circuit closure, outlet for attachment of timer obtained from regular portable roentgen machine, and voltage and "kilovoltage" meter connections.

The knife switch is incorporated to demonstrate a simple timer device. A similar knife switch is found in the autotransformer circuit (Fig. 1, No. 1) functioning as a manual timer when the control circuit timer switch is open, demonstrating timing as it was performed in the roentgen unit used in World War I.

The contactor and circuit breaker readily show their protective value with demonstration of line surges and "short circuits."

The control circuit is thus an aid in demonstration of refinements seen in present-day machines.

FILAMENT TRANSFORMER UNIT

The *filament transformer unit* (Fig. 1, No. 5), painted gray, contains a small step-down transformer for supplying current to the "roentgen" tube filament. The filament control is on the panel and governs a small rheostat (illustrated as a choke coil).

For convenience, a step-down transformer with four identical secondary windings supplies the filaments of the rectifier tubes. This is a slight variant from the more common use of two similar step-down transformers each functioning to supply the filament of a valve in the bridge rectifier and a third step-down transformer for the filaments of the remaining two-valve tubes. A control for valve tube filaments is also available on the front side of the panel but it is not turned conveniently without pliers. This control (also a rheostat) so arranged demonstrates the need for occasional filament control of valve tubes for maximum tube life and efficiency.

ROENTGEN TUBE UNIT

The roentgen tube unit consists only of the roentgen tube which in this model is a tungar rectifier with base removed. No increase in demonstration value would result from use of a real roentgen tube whereas definite bodily harm might be incurred through production of high voltage and actual roentgen rays. Certain advantages are offered through the use of a gas-filled tube.

The tungar rectifier has an appearance quite similar to a basic roentgen tube. Filament control is readily visualized and the photoelectric effect of electron emission is effectively demonstrated when the timer switch is closed. With the insertion of resistors in the "high tension" circuit (Fig. 2, No. 6) both voltage and milliamperage waves are demonstrable on the oscilloscope.

To all intents and purposes, the tube used therefore adequately demonstrates a real roentgen tube and has the advantage of safety factors mentioned.

SUMMARY

A model is so constructed that the use of a "live" circuit-diagram is incorporated with the fundamental working parts of a basic roentgen machine (high voltage transformer excepted). Through the use of snap-fastener connections at all important points, the diagram is "live" electrically for the demonstration of fundamental teaching problems.

The circuit is divided into basic units through the use of colored panels. Circuit connections can be varied between panels. For further versatility, the rectifier panels are interchangeable, resulting in a teaching aid with three or more demonstrable types of roentgen machines.

We believe that this demonstration roentgen machine will prove of value in other army and civilian hospitals and teaching centers. It is of simple construction and many parts can be obtained from old radio or electrical equipment. Other parts can be designed and built to fit the needs of the machine.

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EQUIPMENT DATA

- M_1 —100 ma. meter (also used as voltmeter and "kilovoltmeter")
- O_1 —Standard two-pole convenience outlet
- R_1 } —750 ohm-5 watt resistors (equivalent to
- R_2 } one 1500 ohm-10 watt resistor)
- R_3 —2000 ohm-12 watt resistor

- R_4 —500 ohm-50 watt potentiometer with knob control
- R_5 —500 ohm-50 watt potentiometer with screw control
- R_6 } 2500 ohm-12 watt resistors
- R_7 }
- S_1 } —Five position wafer switches
- S_2 }
- S_4 —Three pole-three position wafer switch
- S_3 } —Single pole-single throw knife switches
- S_6 }
- S_5 —Double pole-single throw fusible knife switch
- T_1 —150 volt autotransformer (see winding data)
- T_2 —High voltage transformer (dummy)
- T_3 —Filament transformer for rectifier tubes (see winding data)
- T_4 —Filament transformer for simulated roentgen tube (see winding data)
- RL_1 —Circuit breaker
- RL_2 —Contactor
- V_1 }
- V_2 } —Vacuum tube rectifiers, type IV.
- V_3 }
- V_4 }
- V_5 —Simulated roentgen tube (tungar rectifier with base removed)
- Snap fasteners
- Power cord and plug
- Switch and rheostat knobs
- Lugs for soldered connections
- Copper hook-up wire
- Miscellaneous nuts and bolts
- Two pairs of meter leads with snap tips
- Two pairs of oscilloscope leads with snap tips
- Oscilloscope (separate unit)
- Hand timer (separate unit)

Each transformer is wound to fit the specific plans for a demonstration machine. Wire sizes are not too important, and like most other parts, are dependent upon what is available.

The autotransformer (T_1) was constructed from core and shell of a "burned out" 40 watt radio filament transformer.

Winding procedure: No. 30 enameled copper wire (a larger size may be used) is wound—four turns per volt—with taps brought out as follows: (1) start; (2) 80 turns; (3) 160 turns; (4) 240 turns; (5) 320 turns; (6) 480 turns; (7) 520 turns; (8) 540 turns; (9) 560 turns; (10) 580 turns; final tap at 600 turns. Of these, five are used as primary taps and ten as secondary taps so it is seen that four taps do double duty. This is accomplished by connecting one

side of the A.C. supply to tap (2) and *not* to tap (1). The other side of the A.C. supply is fitted with a snap fastener which is connected to tap (11) for 130 volts line voltage; to tap (9) for 120 volts; to tap (7) for 110 volts; and to tap (6) for 100 volts. Taps (1), (2), (3), (4), and (5) are connected to the five positions of the major adjustment switch. Taps (7), (8), (9), (10), and (11) are connected to the minor adjustment switch.

With the primary line voltage compensation (primary taps) set to corresponding line voltage, it is possible to vary secondary voltage from 50 to 150 volts in five volt steps.

The *filament voltage transformer* (T_3) for the rectifier tubes is wound to the following specifications:

Core and shell—salvaged from a small radio filament transformer with a "burned out" secondary (here again a 40 watt transformer is satisfactory).

Primary winding—used without modification.

Secondary winding—The old secondary winding is carefully removed and turns are counted. From these data and secondary voltage rating it is determined that the turns per volt should be 5.5. Then four identical secondary windings are wound over the primary using 40 turns of No. 22 enameled copper wire for each winding.

This results in a voltage slightly above the 6.3 volt rating of the 1 V tubes but this voltage could be dropped by means of resistance R_4 (Fig. 2). Separate leads are brought out from each secondary winding.

Turns per volt will vary with type of transformer obtainable.

The *filament voltage transformer* (T_4 —Fig. 2) for the simulated roentgen tube is wound in a manner similar to that used in winding transformer T_3 . In this instance, however, the turns per volt figure is 5.0 for the single secondary coil wound.

Secondary winding—The secondary is wound with a pair of No. 14 enameled copper wires to insure enough current capacity.

(A single No. 12 or larger enameled copper wire would be satisfactory to supply the 15 amperes drawn by the tungar rectifier but No. 14 wire is more easily wound than either No. 12 or No. 10 wire.) The winding is made with 12 turns which give an output of 2.4 volts with 120 volts on the primary side. Secondary voltage is controlled by R_5 (see Fig. 2).

A PORTABLE VIEWING BOX AND DISPLAY CASE

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THE piece of equipment described below performs a double function without loss of efficiency for either purpose.

As a roentgen-ray viewing box, it accommodates six 14×17 inch films or an equivalent surface area of smaller ones. As a display case, it provides space for one hundred standard lantern slides or four hundred 35 mm. mounts or any desired combination of the two. As part of a physician's office furniture, one-half may be used as a roentgen-ray viewing box and the other half for an exhibit of interesting

front. On the bottom, the strips are of equal dimension, but reversed in position. Three hinges are then provided for the top and a pair of strong clasps for the bottom. Two struts are fitted to the bottom so as to project 5 inches beyond the edge at the back. They should be attached by a single large screw or bolt, so that they can be swung under for the sake of portability. When the box is opened, it presents a plane front $42\frac{1}{4} \times 43\frac{1}{4}$ inches sloping backward, a total of 3 inches from the vertical.

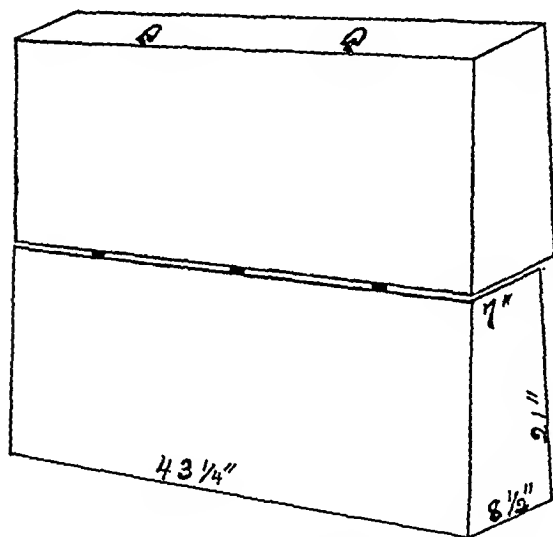


FIG. 1. This shows the outline with measurements in inches.



FIG. 2. A photograph of the case being used as a viewing box in the upper section and as a permanent exhibit of Kodachromes in the lower.

or attractive transparencies. In this way, it is useful and decorative at the same time.

Since its construction is not beyond the ability of any good workman, the rough blueprint data are provided herewith. The box measures $43\frac{1}{4} \times 21 \times 15\frac{1}{2}$ inches and is made of $\frac{3}{4}$ inch lumber, preferably of light weight. It is placed in such a position that the $15\frac{1}{2} \times 43\frac{1}{4}$ inch surfaces form the top and bottom. Then it is cut lengthwise on the bias leaving, on the top, a 7 inch strip at the back and an $8\frac{1}{2}$ inch strip at the

The entire box is painted white on the inside. Each half is measured off in three equal sections and, in each section is installed a pair of sodium vapor lights of 15 watt strength and 18 inches long. The lights are backed by a continuous sheet of metal, shaped to form a curved reflector for each pair. The metal surface is then painted white. Detailed data for the installation of the lights and reflectors are not given, since they can be obtained from

any standard modern roentgen-ray viewing box.

A framework of supports is affixed and the enclosure is completed by a single sheet of triple-flash opalescent glass for each section.

A removable holding frame and panel is built for each section. The frames are provided with suitable springs on the upper borders to hold roentgenograms in position. The panels consist of six grooved strips laid upon cross pieces so as to accommodate five rows of ten standard lantern slides each—a total of one hundred for the two sections. If 35 mm. film is to be

used, four exposures can be mounted between a pair of standard cover glasses. The lantern slides are inserted by sliding them along the grooved channels from the left hand end, and the entire panel, when thus set up, may be inserted into its proper section instead of the roentgen film holding frame. It is secured by wing buttons. The case may then be closed and the prepared exhibit easily transported by automobile without danger of breakage. In order to set it up, it is only necessary to open the case and plug into a source of electricity.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

SKELETAL SYSTEM

BIANCHI, ANDRÉS, and MUSCOLO, DOMINGO. Limfosarcomatosis con lesiones óseas. (Lymphosarcomatosis with bone lesions.) *Rev. ortop. y traumatol.*, Oct., 1943, 13, 79-94.

Virchow in 1864 differentiated lymphosarcomatosis from the large group of leukemias but he also included malignant granuloma under this name. Kundrat in 1893 differentiated it from lymphogranulomatosis. By changing Virchow's name of lymphosarcoma to lymphosarcomatosis he defined its systemic character. Sternberg made a careful histopathological study of lymphosarcomatosis and established the differences between it and the leukemias and also between it and the true malignant tumors.

The disease generally begins in Waldeyer's lymphatic ring or in the mediastinal or retroperitoneal glands. It affects a whole group of glands from which it extends directly by propagation or more rarely by way of the lymphatic to other glands. The capsule soon breaks down and the glands become adherent to each other. All the surrounding tissues are infiltrated. The spleen is not affected and though the liver is involved the lesions are never so great as in lymphadenosis, which is an important differentiating sign. The vessels are surrounded and compressed but rarely infiltrated. The kidney is frequently affected and greatly enlarged.

A case is described in a young man seventeen years of age who first came for treatment for swelling of the submaxillary glands; the process extended to the mediastinal, abdominal and inguinocrural glands and to various bones. It was extremely malignant and the patient died in less than a year. Photographs, roentgenograms and microphotographs of the histopathological findings are given. The nodules in the kidneys and the tissue which surrounded the vena cava showed, as usual, that the lymphosarcomatosis had infiltrated the tissues without causing the destruction characteristic of malignant tumors. The process had spared the glomeruli and renal vessels as well as the vena

cava. The compression of this vessel with marked reduction in its lumen had caused the great edema of the lower limbs.

Roentgen treatment was given and the growths proved very radiosensitive but the process was so diffuse that it could not be arrested permanently.—Audrey G. Morgan.

PAVLOVSKY, ALFREDO, PATERSON TOLEDO, R., and MUSCOLO, DOMINGO. Linfogranulomatosis ósea; comentarios sobre 25 observaciones. (Lymphogranulomatosis of bone; comment on 25 cases.) *Rev. ortop. y traumatol.*, Jan., 1944, 13, 136-157.

Malignant lymphogranuloma or Hodgkin's disease is a pseudoleukemic disease belonging to the group of granulomas. It is generally classified as local or generalized but the authors use a classification into tumoral, infectious and mixed forms.

Sometimes the bones are involved. Among 402 cases seen by the authors there was bone involvement in 25, or 6.21 per cent. Occasionally the bone symptoms are primary. This was true in 4 of these cases. In all these the bone lesions were located in the sternum and biopsy material was obtained by puncture. It is probable that bone lesions are not visible roentgenologically at first as autopsy material shows a much larger proportion of bone lesions than does roentgen examination.

In 40 to 48 per cent of these cases bone involvement was a premonitory sign of death, but the authors believe that this is because the bone lesions usually appear late rather than that they add to the malignancy of the disease. However, in 3 cases the appearance of the bone lesions coincided with a change of the disease from a tumorous into an infectious form, with frank acceleration of malignancy and the beginning of cachexia. Various bones were involved in this series but the most frequent involvement is in the lumbar column and pelvis or the dorsolumbar column and ribs. In 2 of the cases the lymphogranulomatosis was associated with tuberculosis, in 1 case with Pott's disease and in the other with pulmonary and gland tuberculosis.

The roentgen characteristics of the bone

disease are discussed and illustrated with many roentgenograms of the different forms. A table is given showing the clinical features of the cases.

In the early tumoral stage, roentgen treatment is very effective but when the disease has taken on an infectious character it is ineffective.

In spite of the severity of the involvement of the vertebrae in some cases, the spinal cord and nerve roots are rarely affected; they were involved in only 4 of this series of cases. When the cord is affected it is generally by pressure from extrameningeal tumors rather than by infiltration of the meninges and cord.—*Audrey G. Morgan.*

BROCKLEBANK, J. A. Focal osteitis fibrosa of the skull. *Brit. J. Radiol.*, Feb., 1944, 17, 62-63.

A man of twenty-eight came for examination on account of headaches and an asymmetrical swelling of the face. He said the asymmetry and swelling in the right zygomatic region had been present as long as he can remember but in the last six months there had been a marked increase in size. His general health was good and the rounded tumor of the right cheek had displaced the eye upward and the corner of the mouth downward. There were similar tumors in the right temple and occiput, all painless. His facial appearance suggested trigeminal palsy on the right side but there was no muscular weakness nor disturbance of vision.

Roentgen examination showed dense sclerosis of the basal bones and great hyperostosis of the frontal, occipital and right parietal regions and the right maxilla. The whole of the skull showed many woolly patches which suggested osteitis deformans. There were cystic lesions in the pelvis and femurs.

Major J. Duncan White said that this was apparently a case of osteitis fibrosa. The cystic areas resembled those seen in hyperparathyroidism but this disease generally occurs in elderly women and this patient had no clinical symptoms of excessive endocrine activity. Quite frequently in osteitis fibrosa there is thickening of the vault of the skull which sometimes greatly resembles that seen in osteitis deformans.—*Audrey G. Morgan.*

FOLLIS, RICHARD H., JR., and JACKSON, DEBORAH A. Renal osteomalacia and osteitis fibrosa in adults. *Bull. Johns Hopkins Hosp.*, April, 1943, 72, 232-241.

This report concerns the autopsy findings in the vertebrae of 39 patients who died of renal insufficiency. The authors found that approximately 50 per cent of these patients had skeletal lesions. The most predominant finding was the presence of excessive osteoid tissue, justifying a diagnosis of osteomalacia; in a lesser proportion the changes of osteitis fibrosa cystica were found. The lesions were present more often in cases of chronic glomerulonephritis or pyelonephritis than in chronic vascular nephritis. They attempt no explanation of these skeletal changes because of the complexity of the problem and the difficulty in correlating such variable factors as blood serum protein, calcium and phosphorus, and the influence of the parathyroid hormone.

They refer to reports by Ginzler and Jaffe, Bergstrand, and Mach and Rutishauser that one can recognize histological alterations in the skeletal system of adults having renal insufficiency before they manifest themselves clinically or by roentgenological studies, but do not present evidence to support or disprove this contention.—*Angus K. Wilson.*

GUNTHER, LEWIS, COHN, ELMA T., COHN, WALDO E., and GREENBERG DAVID M. Metabolism of bone salts in resistant rickets; report of a case, with balance and radioactive studies. *Am. J. Dis. Child.*, Nov., 1943, 66, 517-527.

This paper is the report of an investigation of the fate of labeled radioactive phosphorus and of the total calcium, magnesium and phosphorus balance in a case of intractable rickets. The patient was a boy who suffered from rickets from infancy until fourteen years of age in spite of treatment with vitamin D and supplements of calcium salts. The disorder was corrected by the daily administration of fish liver oil high in vitamin D. The dose started at the level of 122,000 U.S.P. units per day and was eventually reduced to about 50,000 units per day.

Studies of mineral metabolism showed that a positive calcium and phosphorus balance could be maintained only when the intake of these elements was high. Otherwise both the calcium and phosphorus balances were negative. The changes in the balances corresponded to changes in the amounts of the minerals excreted in the feces. The urinary excretion of both calcium and phosphorus remained practi-

cally unchanged with either high or low calcium diets.

Tracer experiments with radioactive phosphorus showed that phosphate was readily absorbed from the intestinal tract by the patient. The hypothesis is offered by the authors that the primary defect in this condition is not failure of absorption of the bone salts but rather in a failure of the calcifying mechanism.

The paper is illustrated with serial roentgenograms showing the rachitic changes in the bones at various intervals during the course of treatment.—*R. S. Bromer.*

FOLLIS, RICHARD H., JR., JACKSON, DEBORAH, ELIOT, MARTHA M., and PARK, E. A. Prevalence of rickets in children between two and fourteen years of age. *Am. J. Dis. Child.*, July, 1943, 66, 1-11.

Two hundred and thirty children aged between two and fourteen years who died in the Harriet Lane Home from all causes were examined in consecutive autopsies for rickets. The total prevalence of rickets was found to be 46.5 per cent. The figures according to years indicated that the disease occurred with scarcely diminished frequency up to the fourteenth year. In 23 per cent of the total number studied the disease was classified as slight, in 18.7 per cent as moderate and in 4.8 per cent as advanced. In the white children the total prevalence was 43.6 per cent and in the Negro children 48.5 per cent. The prevalence of the disease in well developed degree was greater among Negro children.

No definite relationship between the occurrence of rickets and any particular disease could be established, with the possible exception of chronic lead poisoning. The prevalence of rickets among children dying of acute disease was greater than among those dying of chronic disease. The authors regard the significance of this as not clear. Disease may favor the development of rickets or, on the other hand, interfere with or actually block its development.

The greatest prevalence of rickets was in the winter months, December to February; the lowest, in the autumn months, September to November.

The fact is emphasized that the authors' studies dealt with a hospital population, not with the population at large. However, their

study suggests strongly that rickets is a frequent occurrence in healthy-appearing children.

It was possible to recognize rickets by means of roentgen examination at most in 5 cases. They consider this fact not remarkable, since the characteristic roentgenographic signs are those which develop at the cartilage-shaft junction and changes there are apt to be confined to so narrow a stratum in children three or four years old. Because of the slower growth they do not show clearly. In still older children the changes at the cartilage-shaft junction may not develop at all, even though the shaft may be the seat of advanced involvement. With at most 5 exceptions, the rickets in the older children studied in this report could have given no outward signs of its presence.

The bones studied were the middle ribs.

The authors were totally unable to use Schmorl's classification of "beginning," "florid," "healing" and "healed" rickets, and they do not believe it is sound. They could not regularly differentiate between "beginning" rickets and slight rickets which had been present for a long time but had remained in a state of only slight development. They could also not distinguish between "healing" rickets in many cases and a very common form of the disease in which a healing process is operative all the time but never becomes sufficient to end the disease. They made no attempt to note those cases in which the rickets had entirely healed and only deformities were left.—*R. S. Bromer.*

KUHN, HAROLD H., and HEMPHILL, JAMES E. Baker's cyst: posterior herniation of the knee joint. *Radiology*, March, 1944, 42, 237-240.

Baker described 10 cases of these synovial cysts and differentiated them from diseases of the knee joint. He at first believed they were the result of osteoarthritis. In 3 of his patients there was a true herniation through the posterior wall of the joint capsule.

These hernias usually develop gradually. With the patient upright and the knee extended the cystic swelling appears as a bulging mass on the medial aspect of the popliteal area distal to the popliteal skin creases. There is a soft, tender, non-fluctuating mass along the lateral aspect of the semimembranosus tendon. Differential diagnosis must be made from lipoma, hyperplastic bursitis, fibrosarcoma, angioma and arteriovenous aneurysm.

Diagnosis is made by injecting air into the joint and bandaging the lower third of the thigh so that the air is forced into any cyst that may exist. Roentgenograms with soft tissue exposure are then made. Two cases are described and roentgenograms given.

If these cysts are small they may be treated with a tight binder and a pressure pad over the mass. If they are large enough to cause edema of the leg or interfere with the normal motion of the knee joint they should be removed surgically. If there is a pedicle it should be followed into the knee joint and its intra-articular part severed. The capsule is then closed completely which minimizes the possibility of recurrence.—*Audrey G. Morgan.*

HAUCH, PAUL P. Pneumoroentgenography of the knee joint. *Brit. J. Radiol.*, March, 1944, 17, 70-74.

Strenuous training for military service has resulted in many injuries of the knee joint. Clinical examination can be usefully supplemented by roentgen examination of the joint after aspiration and the injection of 100 to 140 cc. of oxygen. An elastic bandage is applied tightly above the joint to force the oxygen into the lower compartments. The patient lies face downward with knees slightly flexed and films are made of each joint space in the anteroposterior position and in internal and external rotation. Forced adduction and abduction are applied in securing films of the internal and external spaces. Oxygen is used in preference to air as it is absorbed more quickly. No infection has followed the use of the method in any of the author's cases.

A series of 21 cases is reported with roentgenograms showing the normal appearance of the joint and various abnormal conditions. In 11 of the cases torn menisci were found. Other pathological conditions found were hypertrophied fat pads, loose bodies, Pellegrini-Steida's disease, discoid cartilage and postoperative absence of menisci.

Further development of this method will doubtless prove of great value in diagnosing cases of injury of the knee joint that cannot be diagnosed clinically. It will be even more accurate if there is close correlation of the clinical, operative and roentgen findings.—*Audrey G. Morgan.*

MAROTTOLI, OSCAR R. Sobre las fracturas de la apófisis externa del astrágalo. (Fractures of

the external tuberosity of the astragalus.) *Rev. ortop. y traumatol.*, Oct., 1943, 13, 107-117.

Fracture of the external tuberosity of the astragalus is extremely rare, only 6 cases having been published before this article was written. The publication of these 4 cases is justified by this rarity and by the fact that the lesion is often incorrectly diagnosed as sprain and the late results may lead to suits for damages.

The anatomy of the astragalus and its articulations is reviewed. The clinical signs of this fracture are inability to walk, marked edema of the ankle, ecchymotic infiltration of variable extent around the region of the external malleolus and an intensely painful point in front of and a little above the vertex of the external malleolus. A roentgenogram shows the tuberosity broken off at the level of the vertex of the external malleolus or only the most projecting part of the tuberosity may be detached. This form may be caused by strong traction on the ligaments. Generally there are no other bone lesions but in one of the author's cases a small fragment was broken off from the external malleolus and the internal malleolus was fractured, while in another there was incomplete fracture of the lower third of the tibia.

Four cases are described and illustrated with roentgenograms and photographs of operation. The fractures were caused by falling from a height and striking on the feet, or in 1 case by being struck by an automobile. In 2 of the cases a mistaken diagnosis of sprain had been made and the patients did not come to the author until nine and five months after the accident. In both these cases operation had to be performed and the detached part of the bone removed. In the other 2 cases the patients came for treatment immediately after the accident and consolidation was brought about by the application of a plaster cast and the use of Braun's apparatus.—*Audrey G. Morgan.*

SCHEARER, W. S. Ainhum. *Brit. J. Radiol.*, Jan., 1944, 17, 25.

A case in an Indian soldier is described and illustrated with a roentgenogram. The fifth toes on both sides were greatly swollen and constricted at the base as if a tight ligature had been tied around each one. The shafts of the first phalanges of the fifth toes were narrowed

and the second and third phalanges of the fourth and fifth toes were fused. The cause of this disease is unknown. It occurs usually in dark races and the essential feature is constriction of the base of the small toe, and is almost always bilateral. The name comes from a native word meaning to saw or cut.—*Audrey G. Morgan.*

GENERAL

BAYLIN, GEORGE J. Body section roentgenography. *South. M. J.*, August, 1944, 37, 418-424.

The author, in a well-arranged and excellently illustrated presentation, considers the application of body section roentgenography for the elucidation of lesions which are obscure or impossible of detection by conventional roentgenographic methods. He has found the procedure especially useful in demonstration of post-thoracoplasty cavity, bronchial tumors, bronchiectasis, the temporomandibular joint, tumors of the larynx and nasopharynx. He has been able to show sequestra in osteomyelitis of the femur when conventional methods failed because of density of bone, and he has obtained lateral roentgenograms of the thoracic spine free from objectionable shadows of superimposed parts. He concludes that the method has a definite and firmly established place in the roentgenologist's armamentarium.—*Angus K. Wilson.*

VALLS, JORGE E., and SCHAJOWICZ, FRITZ. Tuberculosis muscular hemat6gena. (Hematogenous muscle tuberculosis.) *Rev. ortop. y traumatol.*, Jan., 1944, 13, 158-173.

Tuberculosis in muscle is generally secondary by direct propagation from bones, joints, tendons, etc. Its hematogenous transmission from foci at a distance is rare and a true primary tuberculosis of muscle can be brought about only by direct inoculation. Only a few cases of hematogenous tuberculosis have been described and those mostly in the German and Italian literature. This is probably because the disease is better known in those countries and it is doubtless often overlooked in countries where the picture is not known.

For this reason the authors give a detailed description of a case in a young woman of twenty-three who was admitted to the hospital with the picture of pulmonary tuberculosis. The right shoulder joint showed moderate

muscle atrophy, limitation of movement and pain on movement of the arm. An abscess developed in the upper part of the arm and opened spontaneously. Later pain developed in the sacroiliac joint and a tumor of the anterior surface of the left arm. This tumor was operated on and proved to be a caseous mass in the muscle. Histopathological examination and animal inoculation proved it to be tuberculous. A photograph of the specimen and microphotographs of the histopathological findings are given.

Diagnosis of tuberculosis of muscle is difficult and is generally made only on operation. Treatment is surgical and cure can generally be brought about by removal of the foci even if they are multiple. Some authors recommend postoperative roentgen therapy. If the local condition of the focus and the patient's general condition do not permit of operation, evacuator puncture, roentgen therapy and general treatment may be used. The prognosis of the solitary form is good; that of the generalized form depends on the condition of the original lesion and the patient's general health.—*Audrey G. Morgan.*

COLVIN, S. H., JR., GORE, IRA, and PETERS, MICHAEL. A case of histoplasmosis (Darling) with autopsy *Am. J. M. Sc.*, March, 1944, 207, 378-385.

A study of the literature and a review of their own case leads the authors to conclude that histoplasmosis may be suspected when a patient presents continued fever, leukopenia, splenomegaly, hepatomegaly, anemia, lymphadenopathy, skin lesions and gastrointestinal ulceration. Clinically, however, the last three features were not present in this case, a colored male, aged twenty-three, whose occupation was a laborer and whose home was in Alabama. The diagnosis was not made before death and this has led the authors to point out several critical steps that may be taken in establishing a diagnosis. The more common diseases must be ruled out before considering the rarity. In the present case the clinical picture was confused by a roentgen diagnosis of miliary tuberculosis with which the finding of nine specimens of sputum negative for acid-fast organisms was not incompatible. It is thought that fungus was probably present in the sputa of this patient and if suspected could have been demonstrated by smear or culture. Again, more careful blood

studies, cultures, or bone marrow examination could have led to an ante mortem diagnosis as made in some of the previously reported cases. Biopsy of enlarged lymph nodes or of granulomatous skin, nasopharyngeal or gastrointestinal lesions constitutes the remainder of the diagnostic armamentarium.

The presence of anemia and leukopenia in histoplasmosis may be beautifully explained by the bone marrow findings in the present case as a quantitative reduction of the hematopoietic marrow by multiple granulomatous lesions which displace it. The presence of rather marked marrow hyperplasia between the granulomatous foci would speak against any marked toxic effect of the systemic infection.

Culturally the fungus grows as a yeast at 37°C., and produces mycelia with aerial hyphae at room temperature. Experimentally both forms are pathogenic but the mycelial form reverts back to the yeast form in tissues.—*James J. McCort.*

ROENTGEN AND RADIUM THERAPY

IRA I. KAPLAN, One year observations of the treatment of cancer with avidin (egg white). *Am. J. M. Sc.*, June, 1944, 207, 733-743.

This article is the report of a clinical test based on the hypothesis that cancer cells require biotin for their metabolic function and that egg white might seriously interfere with the vital function of malignant cells and thus bring about their destruction. This hypothesis was based on the observation of the close influence of biotin on cellular growth and that egg white or, more precisely, its constituent, avidin, possesses the ability to deprive the human system of biotin and thus possibly inhibit the influence of biotin on abnormal cell growth. In the experiments carried out each patient ate 36 to 42 egg whites per day with a general diet as free as possible from food rich in biotin along with a daily supplement of accessory vitamins and minerals. No untoward effects resulted from this diet and, as a whole, the general condition of the patient was markedly improved.

Eight case reports are given in some of which the malignancy showed a slight regression or the growth of the tumor was thought to be retarded. The cases selected were those that could readily be visually and clinically identified and the changes, if any, readily recognized.

All cases were proved by pathologic study to be malignant.

The author states that as yet no definite cure of cancer has been effected by the use of egg white therapy as employed in this selected group of cases. He feels that as the diet given contained substantial quantities of milk which may have been a source of readily absorbable biotin this may have been one reason for the unfavorable results obtained. They were unable to produce a biotin deficiency in any of their patients. It is thought that an attempt should be made to improve the method of treatment with vitamins so as to balance the diet to such a degree that on the addition of avidin a biotin deficiency would be created.—*James J. McCort.*

BEAN, WILLIAM B., SPIES, TOM D., and VILTER, RICHARD W. A note on irradiation sickness. *Am. J. M. Sc.*, July, 1944, 208, 46-54.

This work was inspired by the discovery that the behavior of the urinary pigments and the codehydrogenases I and II following irradiation of the upper abdomen over the spleen resembled that in severely ill pellagra patients. Roentgen sickness is taken to include the nausea, vomiting, headache, cramps and diarrhea which complicate the course of therapeutic irradiation. It was planned to make a comprehensive investigation of the effect of a standard dose of radiation on normal well fed subjects; upon those given vitamin D deficient diet, with and without supplements of some of the vitamins in which the diet was deficient, and upon pellagrins and upon persons whose poor diet has caused ill health without other stigmata of a specific deficiency syndrome.

The radiation was given in all instances after an over-night fast (thirteen to sixteen hours after eating). An area over the spleen and upper abdomen was used. Four hundred roentgens were administered from a distance of 20 cm., using a Thoraeus filter, 200 kv., 20 ma., at the rate of 33 roentgens per minute.

The results of these studies were as follows: (1) normal persons consuming a good diet or on various vitamin B supplements had no ill effects except nausea in 1 white woman; (2) the syndrome of irradiation sickness in varying degrees of severity occurred in the rest of the patients, including the normal person who had subsisted on a vitamin B deficiency diet for six weeks; (3) roentgen therapy had no unpleasant

effects after nicotinic acid had been given during the last six weeks of a period of more than three months on the controlled diet but a week after the nicotinic acid supplement was discontinued the same amount of irradiation produced the characteristic reaction of roentgen sickness.

In all the cases studied there was a rough but by no means exact correlation between the severity of the reaction and the degree of vitamin depletion as gauged clinically.

Chemical studies showed there was no significant change in the blood level of biotin, pantothenic acid, riboflavin, or nicotinic acid. There was a fall in the cozymase and an increase of the glutathione level. The significance of this remains obscure.

It was concluded from these studies that the optimum time for vitamin therapy is before and not after the syndrome of irradiation sickness appears and that such therapy is essentially preventive in nature. The authors suggest that the basic disorder in roentgen sickness is a disturbance in respiratory enzyme system and point out the fact that since nutrition is often deranged in persons needing radiotherapy, the use of careful dietary and vitamin therapy is logical, if on empiric grounds alone.—*James J. McCort.*

LEDERMAN, M., CLARKSON, J. R., and MAYNEORD, W. V. Rectangular teleradium fields. *Brit. J. Radiol.*, April, 1944, 17, 115-118.

Radium treatment is less readily manageable than roentgen treatment because of the fixed amount of radium and the fixed filtration and because few units are constructed so as to permit of variations in radium-skin distance or in the shape and size of fields. The authors chose certain rectangular fields to be used in the treatment of cancer of the head and neck. The applicators were made in a rectangular form and the dose contours measured by using a number of small condenser chambers exposed at the same time. The doses at given points in such fields can be measured by using the dose finder or the directional caliper. Illustrations of the apparatus and diagrams of its method of application are given.—*Audrey G. Morgan.*

GOIN, LOWELL S. Low-voltage contact irradiation therapy; further experience. *Radiology*, March, 1944, 42, 241-245.

Five years ago the author discussed the basic

principles of contact radiation therapy and outlined its uses. He now brings his experience with the method up to date. The essential conditions in the treatment are a short distance between the surface and the source of the radiation resulting in the absorption of a large amount of the energy in the first few centimeters of tissue. The depth dose is low. Consequently the treatment must be used for more or less superficial lesions and is not adapted for the treatment of deep-seated tumors.

He uses the Philips Metalix contact therapy unit, 50 kv., 2 ma.; the filtration varies from none at all to 2.5 mm. aluminum, 1.0 aluminum being used most commonly. The total anode surface distance is 22 mm., maximum 42 mm.

He discusses his use of this treatment in papillomas, keratoses, small keloids, small superficial hemangiomas, carcinoma of the bladder and epithelioma of the lip and skin. Very large doses can be given, much larger than in ordinary high voltage roentgen treatment. As a matter of fact the value of a roentgen in this method is probably different from that in other types of roentgen therapy so the doses are not comparable.—*Audrey G. Morgan.*

BUTLER, CARLOS. Cáncer de la mama; tratamiento y resultados. (Cancer of the breast; treatment and results.) *Radiología*, Jan.-Apr., 1944, 7, 1-27.

Early treatment is particularly necessary in cancer of the breast because metastases appear early on account of the abundant lymphatic network of this organ. Therefore a campaign of education of women must be carried on so that they will go to a physician at once on the appearance of any tumor or any other suspicious sign. Such a campaign is being carried on and the number of cases coming for treatment in an early stage is increasing but still a great many cases come after the stage in which cure is possible has passed.

The author discusses 486 cases seen at the Radiological Institute in Montevideo. Of these 187 were in the first and second stages and 299 in the 3d, 4th and 5th stages; 374 had metastases and 112 did not; 420 cases were treated and 66 were beyond treatment. The best treatment is preoperative roentgen therapy, the technique of which is described in detail, followed after six to eight weeks by Halsted's operation with the electric bistoury, and this in turn after about two months by postoperative

irradiation. This treatment should be given in centers with a specially trained personnel and all the equipment necessary for carrying it out effectively.

The results are given in detail; 206 of the patients are dead. Of the patients with metastasis given combined roentgen-surgical treatment 53.3 per cent were cured for one to seven years, 33.3 per cent for more than three years and 13.3 per cent for more than five years. Of those without metastasis treated in this way 66.7 per cent were well for one to seven years, 50 per cent for more than three years and 33.3 per cent for more than five years.

If all cases could be brought to treatment in the first stage of the disease there is no doubt that these figures could be greatly improved.—*Audrey G. Morgan.*

PUENTE DUANY, N., CANIZARES, RAFAEL, and FONTS ABREU, ERNESTO. Cáncer de la mama; tratamiento y resultados lejanos. (Cancer of the breast; treatment and late results.) *Radiología*, Jan.-Apr., 1944, 7, 28-37.

The authors discuss 602 cases of cancer of the breast seen from 1924 to 1937. Of these 100 have been followed up and have remained well for five years or more, 260 died and the rest were lost sight of. The results since 1930 have been much better than those before that time as they have had more adequate roentgen equipment and surgeons better trained in cancerology.

Various factors influence the prognosis, chief among which perhaps is early treatment; if cases could be brought to treatment in Stage I before there are axillary metastases the results could be improved greatly; correct diagnosis is of course essential and the treatment of the patient in an adequately equipped center. Treatment is more effective in older patients than in young ones. Unknown biological factors influence the degree of malignancy of different types of cancer. The scirrhous forms and also the colloidal forms develop slowly. Paget's disease and tumors originating in the excretory ducts show a comparatively favorable course.

The treatment used in these cases was surgery followed by roentgen therapy. Radical operation was performed in the majority of cases, simple mastectomy in some.

Until the cause of cancer of the breast is discovered the only way of improving the results of treatment is by early operation. The governments of all civilized countries should establish

institutes of preventive medicine in all cities and all citizens more than forty years of age should be obliged to go for examination twice, or at least once a year, and special attention should be given to examination of the breasts and uterus in women. The best treatment of cases in Stage I should be studied more carefully and patients kept under observation for ten or fifteen years instead of the usual five years, for recurrences and metastases are often observed after that time.—*Audrey G. Morgan.*

CARVALHO, NELSON. Cancer do seio. Tratamento. Resultados. (Cancer of the breast; treatment; results.) *Radiologia*, Jan.-Apr., 1944, 7, 38-62.

The author insists on the value of a standardized classification of the different stages of cancer of the breast and the working out of the best plan of treatment for each stage. He defines the stages according to Steinthal's classification. Surgical treatment alone is effective in Stage I, but only about 10 per cent of the patients come for treatment during this stage. In this stage the cancer is limited to the mammary gland but this must be proved by microscopic examination. If the axillary glands have already become invaded when the patient first comes for examination, which occurs in 90 per cent of the cases, preoperative irradiation should be given to devitalize the cancer cells, followed by radical operation and postoperative irradiation. The results obtained by surgery alone can be improved by 60 per cent by using combined roentgen therapy and surgery. In advanced cases irradiation alone should be used. Though the results are only temporary they do prolong life and render the patient's life much more tolerable.

Removal of the ovaries cannot be recommended as a routine treatment but improvement is brought about by sterilization in many cases with bone metastases. Each case should be studied carefully and thoroughly before sterilization is advised.

A discussion is given of 71 of the author's own cases which have been under observation for three years. In 68 per cent of these cases three year survival free of symptoms was brought about by combined surgical and roentgen treatment, while surgery alone applied to the same class of cases does not result in more than 25 per cent three year survivals.—*Audrey G. Morgan.*

GUZMAN, LEONARDO. Tratamiento de los cánceres del pecho y sus resultados. (Treatment of cancer of the breast and its results.) *Radiología*, Jan.-Apr., 1944, 7, 63-76.

The types of cancer of the breast are many and varied. Photomicrographs of a number of the forms are given, showing the marked differences in their cell structure. There are also many factors involved in their causation. Practically all of the endocrine glands have an action on the breast and in addition to that there is the factor of hereditary predisposition. It was formerly believed that cancer is at first a local disease that later becomes generalized through the blood or lymphatic circulation. It is now known to be a general disease that becomes localized in organs that are deficient or predisposed for some reason.

A very important point in prognosis is whether the axillary glands have become involved or not. But 15 per cent of glands that can be palpated are found to be free of cancer on microscopic examination and in the same percentage of cases there are microscopic changes in glands that could not be palpated before operation.

Other factors that may be involved in the causation of cancer of the breast are the effect of milk from a cancerous mother, retention of milk which becomes sour and brings about changes in the cells with which it comes in contact; toxic factors from liver disease or chronic constipation or from such diseases as tuberculosis and syphilis; all these factors may cause different types of tumor, depending on which of them act together at a given time on a breast that possibly already has an inherited susceptibility.

At present all these varied types of cancer are treated in the same way and that is probably one cause of the poor results obtained. It is to be hoped that further study will show what types of cancer can be treated by certain hormones or their antagonists, which may be cured by action on the pituitary gland or ovaries, which require surgery, which can be treated by antitoxins, etc. A brief review is given of the treatment at present advocated for different clinical types of cancer of the breast.—*Audrey G. Morgan.*

FRANGELLA, ALFONSO. Consideraciones sobre la roentgenirradiación del cáncer de la mama. (Roentgen irradiation of cancer of the breast.) *Radiología* Jan.-Apr. 1944, 7, 77-79.

Up to 1932 the author used the classical technique of Wintz in the treatment of cancer of the breast at the Radiological Institute of Montevideo but since that time he has used Holfelder's technique because it is better adapted to the anatomy of the breast and being given tangentially spares the lungs and pleura. Four fields are used, two 20×24 and the other two 15×20 or 10×15 cm. The two larger fields extend from the posterior axillary line to the sternal line and the smaller ones also encircle the breast but extend only from what he calls the mammary axillary line to the mammary sternal. The fields are irradiated in turn beginning with doses of 330 r and decreasing to 300, 270 and 240, with a total of 4,500 to 6,000 r depending on the size of the breast and the intensity of the biological reactions. In ulcerative or infectious cases, large doses cannot be given at first because they cause violent inflammatory reactions; a dose of 50 r is given at first, increasing to 100 and 150 r, and when the field is cleansed the larger tumor doses are given. In young women the preoperative irradiation is given in ten to twelve days, the total dose being not more than 3,500 to 4,000 r, in order to avoid very intense biological reactions; the surgeon can operate in three to four weeks.

Postoperative irradiation should not be used as a matter of routine but only in cases of great malignancy and ones in which the axillary glands are invaded. Postoperative irradiation has been called prophylactic but the author does not find that it is so. It is, however, very effective in irradiating involved glands which are more sensitive to irradiation than the original tumor of the breast.

Irradiation is the only effective method of treating generalized bone metastases. Large fields of 50 sq. cm. are used, with doses of about 30 r per day when localized fields are used and 15 to 20 r per day for generalized irradiation. These small doses have a very active effect on the blood picture and the platelet count may be used as a guide to dosage. The intense pain is quickly controlled and though the results are not permanent, the author has had patients who survived three and four years.—*Audrey G. Morgan.*

CAPRIO, GERARDO. Tratamiento radioquirúrgico del cáncer de la mama. (Radio-surgical treatment of cancer of the breast.) *Radiología*, Jan.-Apr., 1944, 7, 80-85.

In the treatment of cancer of the breast in patients from forty to sixty years of age, the author advocates surgery alone in cases that are in Stage I both clinically and pathologically. In cases that are in Stage I clinically but in Stage II pathologically—that is, with microscopic involvement of the axillary glands, surgery and prophylactic postoperative irradiation. In cases that are in Stage II clinically and pathologically, preoperative irradiation, radical mastectomy and postoperative irradiation. In cases in Stage III irradiation alone or in some cases simple mastectomy or electrocoagulation for cosmetic reasons.

In young women less than thirty-five years of age, the results of surgery alone have been discouraging. It is possible that they can be improved by radiotherapy. Teleroentgen therapy offers new possibilities. He does not advocate castration in young women because he thinks the bad psychic effects more than offset the advantages.

Radium treatment is complex and costly and roentgen therapy is to be preferred.—*Audrey G. Morgan.*

TERRIZZANO, MANUEL F., and TERRIZZANO, ARTURO J. M. La castración en el tratamiento radiante del neo del mama. (Castration in the radiation treatment of tumors of the breast.) *Radiología*, Jan.-Apr., 1944, 7, 86-89.

The sex hormones tend to stimulate the growth of cancer cells due to the presence of the phenanthrene group which is also the cancer-producing element in cholesterol and tar. The authors therefore advocate sterilization in the treatment of cancer in young women. Preoperative irradiation of the cancer is given on alternate days with a dose of 400 r, giving a total of 1,600 r in eight days. On the intervening days the ovaries are irradiated from anterior and posterior fields with the same dosage. This is followed after about thirty to forty days by removal of the breast by Halsted's operation. Then after twenty-five to thirty days postoperative irradiation is given up to a total of 4,500 to 5,700 r in a month.

The authors have been using this method with good results in young women for the past five years. The clinical symptoms caused by the castration have not been severe and have been controlled by roentgen stimulation of the anterior hypophysis.—*Audrey G. Morgan.*

CIFARELLI, FRANCISCO P., and PUJADAS, AMADOR A. Sobre los resultados de la roentgenterapia del cáncer mamario. (Results of roentgen treatment of cancer of the breast.) *Radiología*, Jan.-Apr., 1944, 7, 90-92.

The authors use a Stabilovolt-Siemens apparatus, 180 kv., filter of 0.5 mm. copper and 1 mm. aluminum, distance 40 cm. In operated cases they use Wintz' technique, giving a dose of 350 r per day up to 1,750 r. In non-operated cases they use tangential irradiation, increasing the dose and the filter.

Among 151 cases they have treated, only 15, or 9.93 per cent, were in Group I; 106, or 70.2 per cent, were in Group II, and 30, or 19.8 per cent, in Group III. Roentgen therapy alone was used only in Group III. In Groups I and II surgery and postoperative roentgen therapy were used. They have only recently begun using preoperative irradiation and so do not consider it in their results.

All of the patients in Group I are living, some of them after seven and eight years. Among those of Group II 50 per cent are alive after four years, and half of these or more than five years. They have not been able to get reports on some of the cases of Group III and those from whom reports were received were in bad condition.

No changes were seen in the lungs in any of the cases resulting from irradiation. Recurrences were treated with roentgen therapy or surgery with good immediate results. They advocate roentgen castration in young patients.—*Audrey G. Morgan.*

BINNIE, GEORGE G. Regression of tumours following treatment by stilboestrol and x-ray therapy, with notes on a case of breast tumour which regressed with stilboestrol alone. *Brit. J. Radiol.*, Feb., 1944, 17, 42-45.

The author describes 3 cases in which malignant tumors of the breast were treated with a combination of stilbestrol and roentgen irradiation with good results and a fourth in which stilbestrol was used alone, also with marked improvement. This last case was not proved by biopsy to be malignant but he thinks it probable that it was a scirrhus of low malignancy.

The value of stilbestrol in carcinoma of the prostate has been proved and though his cases were all in the breast he believes it will prove equally effective in cancer in other regions and is now trying it. The majority of patients toler-

ate doses of 6 to 10 mg. stilbestrol daily over a long period without any ill effects except nausea and in some women menorrhagia. With continuation of the treatment, the menorrhagia tends to decrease. Some patients have a feeling of well-being in spite of the nausea and many show an increase in weight. The carcinogenic action of stilbestrol need not be considered as the patients already have advanced carcinoma. Radium has a very powerful carcinogenic action but no one hesitates to use it in the treatment of carcinoma. In all of the author's cases except the first one the treatment has extended over several months.

The number of cases is not large enough to justify definite conclusions but the author thinks it worth while to report them to stimulate further trial of the method.—*Audrey G. Morgan.*

McnATTIN, ROBERT F. Treatment of osteogenic sarcoma with preoperative roentgen radiation in large doses. *Radiology*, March, 1944, 42, 246-248.

Early surgery has not proved effective in bone sarcoma. From a study of the literature and his own series of 8 cases, described here, the author concludes that the best treatment is preoperative irradiation followed by surgery as soon as the first signs of irradiation necrosis appear. He gives a long series of high voltage roentgen treatments using 200 kv (peak.), 0.5 mm. copper and 1.0 mm. aluminum filter, half-value layer 0.9 mm. copper, distance 60 to 70 cm. Multiple fields over the lesions are treated, one field daily with 250 to 300 r measured in air. Sixty to 140 treatments are given.

The delay of amputation due to this long series of treatments does not increase the probability of distant metastases. If a metastasis becomes manifest within six months after the beginning of treatment it already existed before treatment was begun. Biopsy is always contraindicated. Osteogenic sarcoma of bones other than those of the extremities should be treated more conservatively as severe irradiation necrosis may be dangerous.—*Audrey G. Morgan.*

LIVINGSTONE, J. L., BROCK, R. C., ROBERTS, FFRANGCON, DOBBIE, J. L., and HARNETT, W. L. Treatment of carcinoma of the lung; symposium. *Brit. S. Radiol.*, April, 1944, 17, 101-109.

Livingstone emphasized the fact that in defi-

nite carcinoma of the lung the outlook is always fatal; but bronchial adenoma is frequently mistaken for carcinoma. He has one such case in which a fatal prognosis was given in 1932 and the patient is still alive and well. Bronchial carcinoma is quite common in men and so far irradiation has been palliative only. The only hope of improving the results is by early and accurate diagnosis. Tuberculosis must be excluded. He has found that cases with bronchial obstruction and infection do not do well under radiotherapy and he does not feel that the improvement brought about by intrabronchial radon compensates for the discomfort caused. He finds radiotherapy particularly useful in the following conditions: In a mediastinal mass which may be Hodgkin's disease or oat-celled carcinoma a rapid decrease in size may be diagnostic; in peripheral tumors, especially when there is great pain; in localized secondary growths in the chest; in postoperative treatment after removal of carcinoma of other organs.

Brock says that the only hope of successful treatment for these patients is surgery. The best method is removal of the whole lung and its lymphatic glands by dissection. Lobectomy is incomplete but may be used in elderly patients in whom total removal of the lung would be too great a risk. He believes the latter operation can be performed in about 10 per cent of patients with bronchial carcinoma. He has performed the operation in 32 cases and 9 of the patients died of the operation, a mortality of 28 per cent. This includes his early cases in which he was experimenting more or less and also includes patients over sixty years of age in whom the operation is particularly dangerous. In reasonably favorable cases the mortality should not be more than 15 per cent. Among the 23 patients who survived the operation there was recurrence in eight. The length of survival in other cases has been up to four and a half years. Graham reports a patient who is alive and working ten years after operation. These patients can do anything but very heavy work after operation.

A very small tumor may cause a large opacity in the roentgenogram, which makes it difficult to determine dosage in roentgen therapy.

Roberts disagreed with Brock with reference to the usefulness of surgery and the uselessness of radiotherapy. He points out that Brock's own reported mortality was high and says

there is no justification for Brock's statement that radiotherapy hastens death. He takes exception to Brock's pointing out the conditions under which radiotherapy should be used and says that that is the province of the radiotherapist and not the surgeon. The latter has only to decide whether he shall operate or not. He considers radiotherapy from the point of view of relief of symptoms, prolongation of life and possibility of cure. Even in advanced cases there may be considerable relief of symptoms. It is hard to estimate the degree of prolongation of life as large series of cases must be considered and each physician or clinic has only a small number. In considering the possibility of cure the characteristics of bronchial carcinoma must be known. A very small tumor may cause a very great disturbance of general health and there is a marked tendency to early dissemination by the blood stream. He formerly used large fields but now uses a double ring of small fields, four in the inner ring and eight in the outer, with a general design somewhat like that of a Tudor rose. With 1,200 r given to each field the total dose may be 28,800 r or even larger. The largest possible dose should be given with the least possible general disturbance. There are no satisfactory figures for depth doses to the lungs. He is now working on the problem. He does not expect any substantial improvement in results from either surgery or irradiation. Any improvement must come from fundamental research and the results will probably be long in coming.

Dobbie reported 170 cases treated by irradiation at the Christie Hospital and Holt Radium Institute from 1935 to 1942. These patients were younger than the usual cancer patients, 9 per cent of them being between thirty and forty. Pain and hemoptysis are the most constant symptoms. He recommends greater use of tomography in diagnosis. He has found bronchoscopy disappointing. Seventy per cent of these tumors were anaplastic. These tumors are unsuitable for surgery. Palliative treatment was given in 111 cases, necessarily with large fields. Twenty-six per cent of these patients lived for more than six months, in some cases with striking symptomatic relief. There was some degree of relief in 40 per cent of the cases. The radical treatment is based on the assumption that many of these tumors are quite small and a large dose is given to a small volume of lung tissue around the tumor. A dose of 6,000 r in five weeks or an equivalent dose at shorter

intervals is prescribed, but too little is known of depth dosage in lung tissue and when a more thorough knowledge of this subject is available the results will probably be better. The author has not found these large doses harmful to the patients. Fifty-nine patients were treated by this method; 11 are alive and 48 dead. Among the dead patients 21 per cent survived for a year or more.

Harnett, who is Medical Secretary to the Clinical Cancer Research Committee of the British Empire Cancer Campaign, reports that out of 15,200 cases of cancer registered in the seventeen months up to September, 1939, there were 1,023 cases of primary bronchial carcinoma. The ratio of males to females was 4.6 to 1, and the average age was 55.9 years for males and 57.7 for females. The cases of bronchial carcinoma constituted 11.5 per cent of all cancer cases in males and 2.3 per cent of those in females. Fifty-nine per cent of these cases were so far advanced when first seen that they were only suitable for palliative medical treatment and 12 per cent were given palliative surgical treatment. Exploration of the chest was made in 5 per cent of the cases but only 1.5 per cent were found suitable for pneumonectomy; 20 per cent were treated with deep roentgen therapy while 1.4 per cent and 2.3 per cent were given intrabronchial radon and interstitial radon treatment respectively. The average duration of the disease in the whole series counting from the time when the first symptoms were noticed to death was 10.2 ± 0.3 months. Taking only the 294 cases in which the disease was judged to be still local the average duration of life was 13.3 months in males and 14.1 months in females. A table is given showing the survival rates in treated and untreated patients.—*Audrey G. Morgan.*

DOUGLAS, S. J. Cancer of the lip. *Brit. J. Radiol.*, June, 1944, 17, 185-189.

The author reports 71 consecutive cases of cancer of the lip treated at St. Anne's Hospital, Dublin, during the year 1939. The incidence of cancer of the lip is high in men engaged in farming and other outdoor occupations, probably because of the frequency of oral sepsis, prevalence of pipe smoking and exposure to wind and sun. The average duration of symptoms before these patients came for treatment was eight months, and in some cases as long as five or six years. It is important that the public

be instructed to come for examination at once when any lump, scaly patch or ulcer appears on the lip. Also that medical students be taught the early appearance of cancer of the lip. Many physicians believe that cancer of the lip is shown only by a large fungating ulcer. If the disease is allowed to reach this stage treatment is almost hopeless.

Of these cases 16 were treated by radium implantation and 46 by contact roentgen therapy. Of those treated by radium 6 were alive and free of disease when last seen. These cases are particularly adapted for contact roentgen therapy. A total surface dose of 8,000 r is given in ten daily doses of 800 r each, treatment being given five days per week. Details of the technique are given. Of these 46 cases 37 are alive and well three years after treatment.

The best treatment for gland metastases is block dissection followed by treatment of the primary lesion. Among the whole 34 cases that showed adenopathy in this group 18, or 53 per cent, are alive and free from disease.—*Audrey G. Morgan.*

KAPLAN, IRA I. Hemangioma of the elbow successfully treated with radium at an early age. *Am. J. Dis. Child.*, May, 1943, 65, 785-787.

Kaplan reports the case of a patient with a hemangioma of the elbow which was treated at an early age, ten weeks. The treatments were given at intervals for a period of eleven months and the patient was followed for a period of nine years. At the time of her last observation the lesion was completely healed and there was no impairment of articular function. There was also no evidence of involvement of bone nor of impairment of epiphyseal growth or of any discrepancy in length of the bones of the treated arm. The radium had been applied directly over the elbow joint, opposite the epiphysis where effects of radium application on the bone are most likely to be noted. Kaplan concludes that fear of adversely affecting growing bones in children with radium therapy are fallacious if irradiation is properly and expertly administered.—*R. S. Bromer.*

BEILIN, DAVID S. Clinical features, diagnosis, and treatment of carcinoma of the colon and rectum. *Radiology*, June, 1944, 42, 539-544.

A series of 117 cases of carcinoma of the colon and rectum is discussed, the oldest patient

being eighty-four years of age and the youngest thirty-two; average sixty years. There were 60 females and 57 males.

Of these tumors 9 per cent were in the cecum, 7 per cent in the ascending colon, 2.4 per cent in the hepatic flexure, 11 per cent in the transverse colon, 8.5 per cent in the splenic flexure, 10 per cent in the descending colon, 22 per cent in the sigmoid, 22 per cent in the rectosigmoid, and 5.9 per cent in the rectum. These figures show that almost half of the cancers of the large bowel are in the pelvic colon.

The most prominent symptom of these cancers of the large bowel is pain, which may or may not be colicky in nature, with diarrhea or constipation. There is often anemia, weakness, loss of weight and a palpable tumor. The average duration of symptoms when the patient came for treatment was about eight months.

There are no pathognomonic symptoms of this condition but the majority of cancers of the rectum and sigmoid can be diagnosed by careful manual and proctosigmoidoscopic examination and the greater part of those proximal to the rectosigmoid can be diagnosed by roentgen examination and the localization determined.

The preferred operation in cases of cancer of the rectum and rectosigmoid is abdominoperineal resection; in those higher up the operations performed were Mikulicz' resection, short-circuit operation, palliative cecostomy or colostomy, or resection with permanent colostomy. The results depend partly on the extent of the disease and partly on the skill of the surgeon.—*Audrey G. Morgan.*

MELBIN, M., and STENSTROM, K. WILHELM. Results of treatment of 173 cases of carcinoma of the rectum. *Radiology*, June, 1944, 42, 545-549.

Eight per cent of all cancers are in the large bowel and half of these are in the rectum.

The authors discuss 173 cases, 69 of which were treated surgically and with irradiation, while 104 were treated by irradiation without operation or with only a colostomy. Five of the surgical group were at first thought to be inoperable but they improved so much under irradiation that operation could be performed. One of these patients in whom the tumor had infiltrated the bladder lived twelve years and died of pernicious anemia without recurrence. In recent years Miles' one stage combined abdominoperineal resection has been the opera-

tion used. Details of the roentgen therapy, which has varied greatly in the course of years, are given. Local radium therapy is generally given after the external roentgen irradiation is completed.

Among the patients treated surgically the five year survival rate was 34 per cent, while among those without surgery or merely a colostomy it was 5 per cent.

Adequate irradiation of cancer of the colon is not merely palliative. The mean life expectancy of untreated cancer of the rectum from the beginning of symptoms to death has been reported as fourteen months. The patients in this series treated by irradiation without operation showed an average length of life of twenty-one months. In a small number of cases cures are brought about by irradiation alone.—*Audrey G. Morgan.*

BORAK, J. Theories on the effectiveness of roentgen therapy in inflammatory conditions. *Radiology*, March, 1944, 42, 249-254.

Since 1926 it has been known that roentgen therapy has a favorable effect on inflammatory conditions even in the most acute stage if very small amounts are given. A dose of moderately filtered rays of from 50 to 150 r has proved very effective in many inflammatory conditions caused by streptococci and staphylococci, gonococci, pneumococci and meningococci. The small dose and the rapidity of its action are the most striking features of this treatment.

This effect has been attributed to a direct bactericidal action of the rays, to an action on the blood, on the exudate and on the blood vessels. Arguments are presented showing that it is not due to direct bactericidal action, or to action on the blood or exudate but to action on the blood vessels. Irradiation does not cause an increase of the antibodies in the blood of the patient but leads to a concentration of the antibodies in a definite area and for a definite time.

It has the effect of both heat and cold but to a milder degree. Like heat it causes a dilatation of the capillaries but like cold it causes a narrowing of the arteries. Like heat it causes retrogression due to resorption through the lymphatics or perforation through the skin from abscess formation. Like cold it lessens the hyperemia and exudation. This combination of effects shortens the inflammatory process more quickly and to a greater degree than can be accomplished by any other conservative method of treatment.—*Audrey G. Morgan.*

POOL, H. H. Roentgen therapy with low dosage in suppurative infections. *Radiology*, March, 1944, 42, 255-257.

The usual dose of roentgen rays in the treatment of infections has been 100 r. As the chief action is on the leukocytes in the inflamed area the author concluded that a lower dosage might be effective in cases in which the inflammation did not recede promptly under this dosage. He therefore reduced his dosage successively to 80 r, 65 r, 50, 35 and finally 25 r. Increasingly better results were obtained as the dosage reached 50 r and below. For the past year he has used 25 r in most cases. Sulfa drugs can be used in association with these low doses without injuring the skin as they cannot with higher dosages.

A table is given showing the treatment and results in 59 cases of various inflammations including axillary abscesses, abscesses of the jaw and neck, mastoiditis, carbuncles, cellulitis, erysipeloid infection, otitis media, infected traumatic wounds, infected operative wounds, abscess of the breast, styes, furunculosis of the ear canal, peritonsillar abscess, acute sinusitis and unresolved pneumonia. The author does not hold that 25 r is the optimum dosage in every case but he thinks that the dose should not be more than 50 r and that 25 r is sufficient in 90 per cent of the cases. He has had excellent results in unresolved pneumonia, in which the treatment should be as in other infections, allowing only for depth. He has had only 1 case of infected traumatic wound but he believes all such cases could be more safely handled with prompter healing if short courses of roentgen treatment were given. This would result in an enormous saving of days for productive effort and much suffering would be prevented. Very little surgery is needed in carbuncles and abscesses with this method of treatment. Nearly 85 per cent drained spontaneously, requiring no incision. Two of the patients with carbuncles were diabetic. The response to treatment was as good as in non-diabetic cases.—*Audrey G. Morgan.*

FREIREICH, KAL. Radiation therapy for obstructing tuberculous hilar lymph nodes. *Am. Rev. Tuberc.*, Jan., 1944, 49, 31-37.

Enlargement of the regional tracheobronchial and bronchopulmonary lymph nodes is an essential component of primary complex pulmon-

ary tuberculosis. Generally, such nodes shrink, fibrose, and calcify without producing symptoms. However, not infrequently the hilar nodes become extremely large, compress the tracheo-bronchial tree, and culminate in obstructive emphysema, atelectasis, and bronchiectasis. Furthermore, a caseous node may invade the bronchial wall thereby producing an ulcerative bronchitis or may rupture into the bronchial lumen, resulting in a massive bronchiogenic tuberculous spread.

Jones, Rafferty and Willis refer to atelectasis produced by tuberculous lymph node pressure as "epituberculosis." They have seen 85 such cases over a five year period. Forty-two of their cases were bronchoscoped, and 17 demonstrated narrowing of the bronchial lumen by external pressure. Ten of the 42 cases died—attesting to the serious prognosis of the condition. Myerson bronchoscoped 29 tuberculous children and 13 showed major bronchial lesions—7 of which were due to lymph node pressure. In his adult group, approximately 1 per cent showed bronchial tuberculous lesions attributable to lymph node pressure.

The author was unable to find a report of a single case of hilar tuberculous lymphadenitis treated by roentgen therapy. He reports the case of a seventeen year old colored girl who entered the hospital in July, 1941, with roentgen evidence of a right pleural effusion and enlargement of the left hilar nodes. A roentgenogram in February, 1942, demonstrated definite narrowing of the left main bronchus just distal to the tracheal bifurcation. Bronchoscopic examination performed in July, 1942, demonstrated a marked widening of the carina; the left main bronchus was narrowed to a slit; and the lumen of the right main bronchus was compressed from without. Despite bed rest, dyspnea increased sufficiently to cause respiratory embarrassment and wheezing became increasingly troublesome. Roentgen therapy was begun in October, 1942. Six treatments of 112 r (200 kv., 0.5 mm. copper filter) were delivered alternately at weekly intervals to the anterior and posterior mediastinum—a total of 336 r being delivered to the anterior and a similar dose to the posterior mediastinum for a total dose of 672 r.

The result was dramatic—after the first treatment, the wheezing diminished and following the third treatment, the dyspnea and wheezing disappeared completely. Roentgeno-

graphic and bronchoscopic studies confirmed the clinical impression of marked decrease in bronchial compression. No adverse effects on the pulmonary tuberculosis were demonstrable during the eight months following treatment.

Radiation therapy would appear to be a safe form of treatment to be tried in certain cases of marked tuberculous hilar lymph node enlargement which threatens to produce severe bronchial compression. This therapy should always be used in consultation with a skilled radiation therapist.—*John R. Hannan.*

MISCELLANEOUS

McCaw, W. W. Training of x-ray technicians at the School for Medical Department Enlisted Technicians. *Radiology*, April, 1944, 42, 384-388.

At the outbreak of the present war there was only one school in the Army for training technicians, that at the Army Medical Center, Washington, D. C. There are now schools at nine Army General Hospitals and hundreds of roentgen-ray technicians have already been trained. The author, working at the Fitzsimons General Hospital in Denver has had an opportunity to observe the results of this training. The course for roentgen-ray technicians now extends over a period of three months, during which time the student is given 504 hours of technical instruction; in addition he is given an hour and a half a day of military training. During the first month he is familiarized with the electrophysical principles involved in the production of roentgen rays, the nature and physical properties of the roentgen-ray beam and the way in which roentgen rays are made use of in roentgenography. The second month he takes up the technique of roentgenography and is instructed in radiography, film criticism osteology and laboratory work. The last month includes a brief introduction to roentgen therapy; lectures are also given on the ethics of roentgen-ray technicians.

Most gratifying reports have been received from radiologists in Army hospitals on the results of this training and the author recommends the establishment of similar schools in civilian practice so that the training program for roentgen-ray technicians may be more or less standardized throughout the country.—*Audrey G. Morgan.*

ROGERS, G. L. Instantaneous stereography. *Brit. J. Radiol.*, April, 1944, 17, 122-125.

Instantaneous stereography is useful in studying the heart, the viscera, arteriograms, phlebograms and possibly the lungs; also in the exact location of radium needle implantations.

The method described here is based on the parallax stereoscope of St. Ives which has been modified for roentgenologic work. The method is promising and worth further development. A figure is given showing the general details which are applicable to both taking and viewing. In taking, the two apices represent the two foci of a bifocal tube or the anodes of two portable tubes run together. Roentgen rays diverge from these points, traverse the object space and are cut up by a grid into thin parallel strips. The apparatus is so arranged that the rays fall on the film in alternate strips, one coming from one anode and the next from the other. In this way the two stereoscopic views are cut up into interdigitating strips. This involves a certain loss of image but in practice the loss is not serious. In viewing, the composite film is placed behind a viewing grid—which can be a photographic replica of the taking grid—and the eyes are placed in a position geometrically similar to the position of the taking anodes. Each eye then sees its appropriate image through the grid. The advantage of this method of viewing over the standard method is explained. Certain avoidable errors in the standard procedure are discussed.—*Audrey G. Morgan.*

MORGAN, RUSSELL H. Reciprocity law failure in x-ray films. *Radiology*, May, 1944, 42, 471-479.

The reciprocity law which is one of the fundamental rules of photography and roentgenography states that the quality of a series of roentgenograms will be uniformly constant if the exposure time with which they are made varies reciprocally with the intensities of the exposing radiation. It implies that, other things being equal, a roentgenogram exposed for 1.0 second with a tube-current of 100 milliamperes will be identical with one exposed for 10 seconds with a tube-current of 10 milliamperes. The law is based on the assumption that the density or blackening of a photographic film is dependent only on the exposure or quantity of radiant energy which the film absorbs and is inde-

pendent of the rate at which the energy is applied, that is, it is independent of the intensity of the exposing radiation. But it has been found that this is not true, but that photographic quality is dependent not merely on the quantity of radiant energy absorbed by the film but also on the intensity of the exposing radiation. The chief significance of reciprocity law failure is its effect on the sensitivity or speed of a photographic emulsion.

The methods of studying reciprocity law failure, its significance and the theoretical considerations on which it is based are discussed and graphs given illustrating the findings in regard to reciprocity law failure in four brands of roentgen films.—*Audrey G. Morgan.*

ELLIS, F., and MILLER, H. The use of wedge filters in deep x-ray therapy. *Brit. J. Radiol.*, March, 1944, 17, 90-94.

In the treatment of deep tumors by roentgen rays it is hard to irradiate the tumor uniformly without injuring the normal tissues beyond it. For this purpose the authors introduce a wedge-shaped absorber into the beam. It is arranged so that the thickness of the absorber increases gradually from one side of a rectangular field to the opposite side so that in any plane at right angles to the central ray the dose is reduced progressively in passing across the field.

Two methods of utilizing the wedges may be used. In the first, two wedge fields are combined at right angles, that is along the adjacent edges of a square, in such a way that the thick edges of the wedges lie along a common line. The second method is used when the distance between two roughly parallel surfaces of the body is relatively small, as in treating the larynx or axilla. In these cases the use of two parallel opposed wedge fields and a direct field at right angles to them gives a very uniform dose distribution. Wooden wedges are very satisfactory for this purpose as the absorption of radiation in wood is very similar to that in tissue. Isodose curves are given for these two methods of use. Descriptions and photographs are given of different types of wedges used.—*Audrey G. Morgan.*

SPENCER, R. R. The place of the National Cancer Institute in the cancer problem. *Radiology*, May, 1944, 42, 493-498.

Thirty years ago the American Society for

the Control of Cancer was launched with the object of educating the public and physicians to understand the importance of early diagnosis and expert treatment of cancer. The activities of this Society resulted in the passage of the National Cancer Institute Act in 1937. The National Cancer Institute, established under this act, provides training in diagnosis and treatment of cancer for a group of young physicians particularly interested in this subject. On completion of their training they are capable of setting up and directing tumor clinics to conform to the standards of the American College of Surgeons.

The National Cancer Institute has purchased 9.3 gm. of radium, about 8 gm. of which has been loaned to hospitals throughout the country for the treatment of cancer patients. No charge is made for the use of this radium and preference must be given to indigent patients. The Cancer Institute cooperates with state health departments in the prevention, control and eradication of cancer. The states endeavor to provide for free or part-pay aid in the diagnosis and treatment of cancer patients, free tissue diagnosis, lay and professional diagnosis and statistical and epidemiologic research, including a system of follow-up of cancer cases. The Institute also prepares films and posters for public education, emphasizing the curability of *early* cancer. In the past five years the Institute has recommended that over \$400,000 be paid to various institutions for research in various phases of the cancer problem, particular emphasis being placed on cancer of the stomach which causes about 25 per cent of all deaths from cancer.

Since 1939 when the National Cancer Institute building was completed the most significant research work has been in the field of carcinogenesis. Some of the details of this work are described and the suggestion is made that cancer may be caused by a process of adjustment of cells to some unusual environmental condition. Work is just beginning on cancer treatment and the development of reliable

tests for the early diagnosis of the disease. Other studies are being made on the metabolism of normal and cancer tissue, the part played in the problem by vitamins and other nutritional factors and by hormones and enzymes. Emphasis is placed on the fact that cancer is a national medico-socio-economic health problem and that it can no longer be left to the individual worker but that the work must be done systematically by organized research groups.—*Audrey G. Morgan.*

PATERSON, EDITH. The time-intensity factor in x-ray irradiation. Part I. The influence of the overall time. *Brit. J. Radiol.*, Jan., 1944, 17, 26-30.

Experiments were made on chick fibroblasts to determine whether the effect of irradiation is influenced by changes in the overall time of irradiation, that is the time from the beginning of the first exposure to the end of the last. During these experiments the total dose and the dosage rate, that is the number of roentgens delivered per minute, were kept constant. Tables are given showing the details of the results. It was found that when the overall time was prolonged the irradiation was more effective, as shown by the fact that both survival rate and survival time were lowered as compared with short-term irradiation. There was also a reduced variation in the time of death so that the survival times were more homogeneous. Nor did the cells show recovery as they did after short time irradiation. The effect was also influenced by the number of sessions into which the dose was split. The effect was greater when the total dose was split into eleven sessions than when it was given in three or four.

These experimental facts do not necessarily hold good in clinical therapy but if they are found to apply there also it would mean that long-term irradiation with suitable splitting produces better effects and shows fewer recurrences than short-term irradiation.—*Audrey G. Morgan.*



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CORRELATION OF GASTROSCOPIC, ROENTGENOLOGIC AND PATHOLOGIC FINDINGS IN DISEASES OF THE STOMACH

AN ANALYSIS OF 245 PROVED CASES*
PANCOAST LECTURE†

By EDWARD B. BENEDICT, M.D.
BOSTON, MASSACHUSETTS

I AM very much honored by the invitation to address this learned society, and I wish now to express my thanks to you and your committee for selecting me to do so. To be included in a list of lecturers with Dr. George W. Holmes of Boston, Dr. Lawrence Reynolds of Detroit and Dr. D. B. Phemister of Chicago is indeed a privilege, and to give a Memorial Lecture in honor of Dr. Henry K. Pancoast, undoubtedly the leading radiologist of his time, marks an important occasion in my medical career.

According to Dr. Pendergrass⁷ the first department of roentgenology in the United States was established by the University of Pennsylvania in 1896, and in 1902 Dr. Pancoast was appointed skiagrapher in charge of this department. Ten years later, he was made Professor of Roentgenology and was elected President of the American Roentgen Ray Society. In 1933 he was elected to the presidential chair of the first American Congress of Radiology, a spontaneous recognition of his long and fruitful life of service to radiology.

I have been asked this evening to discuss the correlation of gastroscopic, roentgenologic and pathologic findings in diseases of the stomach. The word "correlation" is well chosen for it implies cooperation between the three departments and cooperation is the keynote to successful progress. The roentgenologist always has the first chance to examine the patient. If the findings are fairly obvious, he will probably not suggest gastroscopy. The clinician, however, may wish confirmation by gastroscopy. If the roentgen findings are doubtful gastroscopy is always indicated. The pathologist comes into the picture routinely on resected or autopsy specimens. As an indication of the excellent relationship between the roentgenologist and the endoscopist at the Massachusetts General Hospital, I would like to point out that more requests for gastroscopy come from the Department of Roentgenology than from any other source. In other words, gastroscopy is an additional method of examining the stomach, supplementary and complementary to roentgenology, but not in any sense a rival method.

* From the Massachusetts General Hospital.

† Pancoast Memorial Lecture delivered before the Philadelphia Roentgen Ray Society, November 2, 1944.

There is a saying that "comparisons are odious." In the present discourse, however, it will be of interest to draw certain comparisons as to the relative advantages and disadvantages of each method of study under various circumstances. Roentgen examination should always be performed first not only because it is easier and safer but also because it gives indispensable evidence regarding the esophagus. Before blindly passing the flexible gastroscope, the endoscopist must be assured of an essentially normal esophageal lumen. Both methods are so comparatively easy, safe and well established that it seems unnecessary to go into any detail regarding technique, indications, or contraindications. The important question before us is that of correlating the results of our studies in gastroscopy, roentgenology and pathology.

For this purpose, out of a total of 1,691 gastroscopies, I have carefully selected 245 cases for study. These are chosen because in each case there has been roentgen examination, gastroscopy, and pathological report. It is noteworthy that in a difficult case the roentgenologist may examine the patient on several occasions, whereas the gastroscopist usually has only one opportunity to make his examination. This is due in part to the relatively more difficult gastroscopic technique and in part to the fact that the gastroscopic method is newer and less well established. The 245 cases studied include carcinoma (125), gastric ulcer (50), duodenal ulcer (25), jejunal ulcer (8), gastritis, (16), benign tumor (7), lymphoma (5), sarcoma (2), metastatic carcinoma (3), normal stomach (4).

CARCINOMA

One hundred and twenty-five cases of proved carcinoma have been included for the purpose of this report. The two methods were equally good 67 times, the roentgenologist demonstrating a fairly obvious tumor mass and the gastroscopist confirming the diagnosis. In 3 cases the methods were equally doubtful, question of ulcer or malignancy in 2 of them, and question of neo-

plasm in 1 case. In 3 cases both were wrong—(1) a proved cancer treated as severe hypertrophic gastritis for two years (a serious mistake, the responsibility for which lies on the writer as gastroscopist and also on the roentgenologist of an outside hospital); (2) a proved cancer missed completely by both methods, and (3) a proved cancer thought to be a benign ulcer. In the remaining 52 cases a more accurate or more valuable report was given by the roentgenologist 32 times, by the gastroscopist 20 times.

An evaluation of these 52 cases is necessarily difficult and perhaps somewhat arbitrary but I believe it will serve to bring out the relative merits of each method. In 25 of the 32 cases where the roentgen ray was more valuable, gastroscopy failed to demonstrate the lesion at all. The reasons for gastroscopic failure in these 25 cases were as follows: (a) obstruction at cardia (7 cases), all due to tumor mass at the cardiac orifice; (b) blind area of the lesser curvature of the antrum (4 cases); (c) prepyloric area not seen (4 cases); (d) lesion in the pylorus not visible (4 cases); (e) spasm of antrum (2 cases); (f) blind area of fundus (2 cases); (g) excessive secretion (2 cases). In other words, some of the mechanical difficulties of gastroscopy are still unsolved. The retrograde objective lens, omniangle mirror, mechanism for proximal control of the tip of the gastroscope, and biopsy forceps have been helpful, but they are limited modifications which have not by any means solved all the problems. For lesions obstructing the cardiac orifice I use the open tube gastroscope with biopsy when possible. Such tumors quite commonly invade the lower end of the esophagus, in which case esophagoscopy may give a positive diagnosis. Even when the lower esophagus appears grossly normal a biopsy may show submucosal extension of the tumor. The transthoracic approach is indicated for tumors in these areas. Owing to the peculiar shape of the stomach, lesions of the lesser curvature of the antrum, prepyloric area and pylorus are more difficult to see than

lesions in the corpus, not only because they are farther from the objective lens but also because they may be hidden around the corner behind the angulus. Certain parts of the fundus may be impossible to see, especially high up toward the lesser curvature. Finally, excessive secretion will obviously interfere with a proper examination.

The other 7 cases where the roentgen examination was more valuable than gastroscopy may be analyzed as follows:

CASE 1. I. F. M. (M.G.H., U No. 95735). On the first roentgen examination the examiner reported an active penetrating ulcer 1.5 cm. long, 0.5 cm. deep on the lesser curvature at the junction of the middle and lower thirds. Three weeks later another roentgenologist reported shortening of the lesser curvature with a 3 cm. crater just distal to the angle of the stomach. Histopathological malignancy could not be ruled out by the roentgenologist who suggested gastroscopic examination. The gastroscopist reported very sluggish peristalsis passing over the antrum and through the pylorus. Several shallow ulcerations were seen on the angulus with reddening, edema and verrucous elevations. The gastroscopic diagnosis was multiple gastric ulcers with superficial and hypertrophic gastritis. Exploratory laparotomy revealed a very extensive inoperable carcinoma involving almost all of the lesser curvature of the stomach. A biopsy taken from the omentum was reported metastatic carcinoma.

Comment. The roentgen examination was definitely superior to gastroscopy in this case. The gastroscopist apparently did not see the large 3 cm. crater beyond the angulus and thought the verrucous appearance of the lesser curvature was due to gastritis. Greater experience and improvements in the instrument in the seven years since this patient was examined might lead to more accurate gastroscopic diagnosis today.

CASE 2. G.R. (M.G.H., U No. 411134). The roentgenologist reported a thickened, elongated rigid pylorus without peristalsis—question of carcinoma. The gastroscopist thought he saw normal peristalsis passing down to a normal pylorus, with a diffuse verrucous eroded mucosa in the body of the stomach and made a diag-

nosis of severe hypertrophic gastritis or lymphoma. At operation a small carcinoma was found about 2 inches from the pylorus. The rest of the stomach showed a marked gastritis.

Comment. The roentgenologist was correct; the gastroscopist may have seen only a prepyloric contraction which he mistook for the normal pylorus.

CASE 3. L. R. (M.G.H., U No. 56379). In this case nine roentgen examinations were made over a period of thirteen months. The report was active gastric ulcer, old duodenal ulcer and hypertrophic gastritis; six months later the crater was markedly decreased in size; a year later "no active ulcer"; thirteen months later old duodenal ulcer and gastritis, suggestion of a shallow ulcerated carcinoma along the posterior wall near the lesser curvature. During this period three gastroscopies were performed, with the following findings: (1) active gastric ulcer with hypertrophic gastritis; (2) no ulcer can be seen, no evidence of malignancy; (3) unsatisfactory due to bleeding.

Comment. After nine examinations the roentgenologist raised the question of malignancy. Gastroscopy at that time was unsatisfactory but the gastroscopist advised surgery because of the persistence of symptoms and inability to work.

CASE 4. A.C. (M.G.H., U No. 343070). In this case the roentgenologist first reported a benign appearing ulcer at the junction of the middle and lower thirds. Three weeks later the large ulcer crater was unchanged in size, there was absent peristalsis, 100 per cent retention, and malignancy was a distinct possibility. The gastroscopist thought the lesion was benign because it had sharp margins and a clean base. At operation, the surgeon believed he was dealing with a benign lesion and the pathologist thought the lesion was benign from the gross appearance. Microscopically "in the mucosa carcinoma is found only in a small zone immediately around the ulcer."

Comment. In this case Schindler's⁹ claim that the presence of the circulating blood enables the gastroscopist to distinguish benign from malignant ulcer was not borne out.

CASE 5. J.G.D. (M.G.H., U No. 338191) The



FIG. 1. Case 7. Roentgen appearance showing one or more ulcerations of the antrum in an area of thickened gastric wall. The roentgenologist was correct in believing this to be probably malignant. The gastroscopist thought the ulcer was probably benign.

roentgen examination demonstrated an organic obstruction in the lower end of the stomach with 100 per cent retention at the end of six hours. The lesion could not be definitely visualized but the findings were consistent with obstructing ulcer or carcinoma. At gastroscopy no peristalsis was seen. Instead of the pylorus there was seen a circular opening, possibly representing a stenosed pylorus, with one erosion and some proliferation but probably not malignant—more consistent with an obstructing ulcer and marked gastritis than with carcinoma.

Comment. This is probably an error in gastroscopic interpretation due to lack of experience, as the examination was made in 1934. It is to be noted also that the roentgenologist failed to see the lesion. This case might well be classified as both methods equally doubtful, but the gastroscopist was in error as he definitely favored a benign lesion.

CASE 6. B.O. (M.G.H., U No. 240438). The roentgen report described a large ulcerated lesion on the posterior wall near the lesser curvature grossly benign (incomplete examination). The gastroscopist failed to see the large ulcer, but reported the angulus 1.5 to 2.0 cm. in diameter remaining in a fixed position. There were multiple areas of ecchymosis, increased reddening, superficial ulceration, edema, and irregular verrucous markings. The verrucous elevations varied in size from 1 to 2 mm. but did not appear sufficiently nodular for a diagnosis of carcinoma to be made.

Comment. The roentgenologist certainly described the important lesion in this case, though he failed to call it malignant. The gastroscopist should probably have thought more seriously about the fixed position of the angulus as an indication of carcinoma.

CASE 7. S.Y. (M.G.H., U No. 334489). The roentgenologist demonstrated one or more ulcerations of the antrum in an area of thickened gastric wall which he thought was probably malignant, possibly lymphoma (Fig. 1). The gastroscopist found multiple gastric ulcers with distortion of the peristaltic wave at one examination but no distortion at a second gastroscopy. He felt it was "probably benign but strongly advised gastric resection." The pathological report was adenocarcinoma in situ with three shallow secondary peptic ulcerations.

Comment. The roentgen examination here had the advantage in demonstrating a thickened gastric wall and an ulcer in the prepyloric area.

In this series of proved carcinomas gastroscopy appeared to be more valuable than the roentgen ray in 20 cases grouped as follows:

- Group A. Roentgen examination: gastric ulcer? carcinoma; gastroscopy: carcinoma (7 cases)
- Group B. Roentgen examination: benign gastric ulcer; gastroscopy: gastric ulcer ? carcinoma (5 cases)
- Group C. Roentgen examination: doubtful; gastroscopy: carcinoma (5 cases)
- Group D. Roentgen examination: polyp; gastroscopy: carcinoma (1 case)
- Group E. Roentgen examination: gastric ulcer; gastroscopy: malignant polyps (1 case)
- Group F. Roentgen examination: gastritis; gastroscopy: carcinoma (1 case)

As an example of *Group A*, I will cite the following:

CASE 8. M.G. (M.G.H., U No. 303682). At roentgen examination the antrum of the stomach showed a large ulceration measuring approximately 3 cm. in length. There was a very marked induration around the ulceration. The condition was considered as probably malignant. Gastroscopy eleven days later showed an irregular ulcer with nodular margins and a white sloughing base on the margin of the angulus. The irregular appearance extended along the lesser curvature below the angulus into the antrum. No peristalsis passed over the lesion. The peristaltic wave was markedly distorted and the antrum was also distorted by this lesion which did not suggest a benign ulcer but which seemed almost certainly malignant. The pathological report was signet ring cell carcinoma.

Comment. In this case, and similarly in the other 6 cases in *Group A*, gastroscopy gave a more complete description of the lesion than the roentgen ray and also a more positive diagnosis.

Group B. There were 5 cases in this group in which the roentgen report was benign ulcer and gastroscopy raised the question of malignancy. The question of carcinoma was raised by the gastroscopist in 1 case (D H., M.G.H. U No. 236117) because of an almost polypoid mucosa close to the ulcer margin, in another (N.G.M., M.G.H. U No 19511) because of slightly irregular margins and a slightly nodular surrounding mucosa "highly suggestive of malignant infiltration." In a third case (W.J., M.G.H. U No. 422778) the angulus was constantly deformed on the lesser curvature by an ulcerating lesion appearing to be about 2.5 cm. in diameter and 1.5 cm. deep with raised edematous slightly ragged margins and a fairly clean gray base: "from the gastroscopic appearance malignancy must be seriously considered." This case was very important as there was an eight year history of mid-epigastric pain relieved by soda, a perforated ulcer surgically repaired two years before entry, and a roentgenogram showing an ulcer crater 2 by 1 cm.—"most

likely gastric ulcer, but I do not believe we can be sure it is not in the duodenum which has been pulled up along the lesser curvature and remains applied to it." In a fourth case (G.E.W., M.G.H., U No. 132669) the gastroscopist believed the ulcer to be malignant because of nodular margins (Fig. 2),

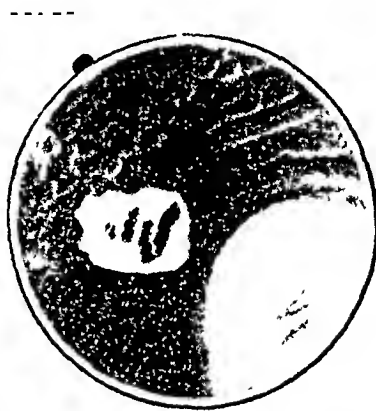


FIG. 2. G.E.W., fourth case in *Group B*. Gastroscopic appearance of ulcer thought to be benign roentgenologically. The gastroscopist reported probable malignancy because of the nodular margins, dirty base, and surrounding nodular mucosa. The pathological report was adenocarcinoma. (Reproduced through the courtesy of Oxford Medicine.)

dirty base and surrounding nodular mucosa. The fifth case in this group is as follows:

CASE 9. M. DeF. (M.G.H. U No. 178371). Nine roentgen examinations were made in twenty-two months and malignancy was never mentioned. The first four reports were large gastric ulcer or active gastric ulcer; fifth, crater much smaller; sixth, slight rigidity, crater no longer visible; seventh, lesser curvature markedly shortened, slight irregularity of lesser curvature but definite ulceration is not seen; eighth, no definite evidence of an active ulcer roentgenoscopically; on the roentgenogram there is slight irregularity of the lesser curvature; there is motion on the roentgenogram, whether this is an ulcer cannot be definitely determined; ninth, ulcer on the lesser curvature larger than at the last examination and reaches almost the same size as at the first examination. Lesser curvature in the neighborhood of this ulcer appears somewhat rigid and edematous. Impression: ulcer of the lesser curvature which appears benign by roentgen examination.



FIG. 3. Case 10. The finding from the roentgen examination was reported as showing no definite evidence of tumor or ulcer. In retrospect, however, this was considered to be an error in interpretation for there is certainly a suspicious area high up on the greater curvature. Large carcinoma in this area was readily demonstrated by gastroscopy (see Fig. 4).

Three gastroscopies were performed during a three month period nine months before operation, with the following findings: (1) benign healing ulcer with chronic gastritis; (2) no evidence of ulceration or gastritis; (3) on the lesser curvature at the angulus was a sharply demarcated lesion with slightly gray base 1 cm. diameter, 3 mm. in depth, consistent with benign gastric ulcer but microscopic malignancy could not be positively excluded. Resection advised. Unfortunately, it was nine months before operation was done. The pathological report was carcinoma with metastases to regional lymph nodes, peptic ulceration of the carcinoma and gastritis.

Comment. This case is of very great importance indicating that a peptic ulcer in a carcinoma may apparently heal completely. Nine roentgen reports failed to suggest malignancy. Grossly the lesion looked benign by gastroscopy but the ques-

tion of malignancy was raised by the gastroscopist on clinical grounds and operation advised.

Group C. There were 5 cases in this group in which the roentgenologist had difficulty in satisfactorily visualizing the lesion due to its location on the greater curvature (2 cases), pyloric obstruction (2 cases), carcinoma close to a stoma (1 case). The following case is an example:

CASE 10. P.H. (B.M. U No. 218126). Roentgen examination showed no definite evidence of tumor or ulcer (Fig. 3). Gastroscopy demonstrated an elevated lesion high up on the greater curvature with soft friable margins and ques-



FIG. 4. Case 10. Gastroscopic appearance of large carcinoma of the greater curvature not reported from roentgen examination (see Fig. 3).

tionable ulceration consistent with carcinoma or lymphoma, presumably carcinoma (Fig. 4). The pathological report on the resected specimen was carcinoma with metastases to the regional lymph nodes.

Group D.

CASE 11. E.V.T. (M.G.H. U No. 341863). Roentgen examination demonstrated a lesion in the lower fourth of the stomach; it appeared to be located within the last 3-4 cm. of the stomach, measured 2 cm. in diameter and was thought to be a small polypoid growth without a stalk. At gastroscopy the pylorus was well seen and on its anterior margin toward the lesser curvature there was a small nodular nipple-like excrescence about 5mm. in diameter and bright red in color. The lesser curvature appeared irregular, indurated and gave a somewhat hard appearance, as though infiltrated.

There was no peristalsis passing over it. There was one slightly depressed area in this region suggesting an ulceration. The greater curvature and posterior wall were very intense red and glistening, showing evidence of a definite gastritis. The rugae were somewhat irregular and tortuous. The gastroscopic findings were consistent with an infiltrating type of carcinoma and a marked gastritis. The pathologist confirmed these findings including a superficial ulcer—adenocarcinoma, acute and chronic gastritis.

Group E.

CASE 12. F. L. (M.G.H., U No. 393564). At roentgen examination the stomach showed a small ulcer at the lesser curvature 1 inch below the cardia. The lesser curvature was not rigid. Peristalsis appeared normal and no filling defects or masses were noted. The findings indicated a gastric ulcer. Gastroscopy revealed multiple polyps; proximal to the angulus on the lesser curvature there was a rather smooth red nodule about 1.5 cm. in diameter and elevated above the mucosa about 1 cm. having the appearance of a polyp. On the greater curvature proximal to the angulus and extending into the upper part of the fundus there were numerous nodules from 0.5 to 1 cm. in diameter. The mucosa elsewhere was somewhat reddened and edematous. The inability of the patient to retain air suggested some rigidity of the gastric wall. The findings were consistent with multiple gastric polyps which were believed to be probably malignant. Because of a nodular liver peritoneoscopy was performed to avoid a laparotomy. Biopsy obtained from a nodule in the liver was reported metastatic adenocarcinoma.

Group F.

CASE 13. T P. (P.H. U No. 435396). Roentgen examination showed prolonged delay in the esophagus with narrowing at the lower end but no rigidity. As the stomach filled, a filling defect appeared on the greater curvature opposite the cardiac orifice—no rigidity. After a fifteen minute delay due to the patient's fainting, the stomach appeared to be of normal shape with normal peristaltic activity. Conclusions—spasm of lower esophagus, probable localized gastritis on the greater curvature. Gastroscopy demonstrated an elevated, irregular polypoid mass about 3 cm. in diameter, looking like a small

fuzzy cauliflower. It appeared to be high up on the greater curvature toward the anterior wall. The examiner concluded that this was probably carcinoma, or less likely hypertrophic gastritis, and advised transthoracic exploration. This was done and a palliative resection performed. The pathologist reported colloid adenocarcinoma of the cardiac end of stomach with extension into the esophagus and metastases to the regional lymph nodes.

Comment. The differential diagnosis between carcinoma and hypertrophic gastritis may be very difficult or impossible by any method of examination. Perhaps the gastroscopist was lucky in this case, perhaps the roentgenologist would have diagnosed carcinoma on a second examination. It should be emphasized that it is far better to explore a patient and find only gastritis than it is to fail to explore a patient who actually has a carcinoma. In doubtful cases, gastrotomy and biopsy should be done.

From the above analysis it is evident that both methods of examination are very important. Where one fails the other may be successful. In 52 out of 125 cases of proved carcinoma one method appeared to be more valuable than the other, the roentgen examination having the advantage by about 3 to 2. Roentgen examination is also an easier and a better established method. The gastroscopist, following the roentgenologist as he almost invariably does, may start with a preconceived idea of the diagnosis, and his observation may be merely confirmatory. Such evidence, however, may be of very great value. On the other hand, it may be a definite handicap to start with a diagnostic prejudice, since it may be erroneous. Besides being confirmatory or otherwise, gastroscopy may add secondary diagnoses such as gastritis with or without erosions or superficial ulcerations. In some cases it may give a more accurate idea of the extent of the lesion.

Carcinoma of the stomach may be classified for our purposes by type and location. The large cauliflower type of tumor is usually readily diagnosed by roentgen examination, and gastroscopic confirmation may

be unnecessary. When, however, such a tumor is located high on the greater curvature in a heavy individual in whom palpation is difficult, or in some cases where there is pyloric obstruction, and other cases where there is distortion from a previous gastric operation, gastroscopy may be the superior method of study. Most of the gastroscopic failures (25 out of 32) were due to mechanical difficulties. In other words, if the gastroscopist can actually get a good view of the lesion the possibility of his being correct is greater than that of the roentgenologist. The latter, however, usually has the advantage in lesions at the pylorus, in the prepyloric area, on the lesser curvature of the antrum, blind area of the fundus, and cases with obstruction at the cardiac orifice. The relative superiority of gastroscopy over roentgenology in differentiating benign from malignant gastric ulcers, when the ulcer is readily visible by both methods, seems to me to be attested by the 12 cases in Groups A and B. In some of these the gastroscopist may have been lucky and in others his clinical judgment may have played a part, for the gastroscopist has a better opportunity than the roentgenologist to get acquainted with the patient and his history. It may be said in passing that since the advent of gastroscopy, roentgen examination of the stomach has consciously or unconsciously received a stimulus which has resulted in more careful roentgenologic technique and more detailed roentgen reports. But we must still not regard the two methods as rivals in any way. In fact, it is amazing how well they supplement each other.

GASTRIC ULCER

Fifty cases of proved benign gastric ulcer have been analyzed as follows: In 16 cases the roentgen ray and gastroscopy were equally correct; in 9 cases equally doubtful; in 21 cases the roentgen examination was superior to gastroscopy, and in 4 cases gastroscopy was superior to the roentgen ray.

As in the cases of carcinoma, the gastroscopic failures were due largely to mechani-

cal difficulties, which accounted for 17 of the 21 cases of superiority of the roentgen examination. Again the mechanical difficulties were chiefly in the prepyloric region (7) and the lesser curvature of antrum (5). It was impossible twice to see ulcers high on the lesser curvature, once near a gastroenterostomy stoma, once the failure was due to excessive secretion and once to spasm of the body of the stomach. In the ulcers well seen by both methods of examination, the roentgen ray seemed superior 4 times, and gastroscopy superior 4 times.

The cases in which the roentgen examination was superior are as follows:

CASE 14. S. E. (M.G.H., U No 338066). At the first roentgen examination there was evidence of gastritis, a spastic antrum, and large duodenal cap—no definite filling defect or ulcer crater. Re-examination was requested and was performed later. Meanwhile the gastroscopist reported on the lesser curvature and anterior wall in the antrum of the stomach close to the pylorus an infiltrating and slightly proliferating lesion about 4 to 5 cm. in diameter which was very red and irregular in appearance, some areas being white. The impression was probable carcinoma of the antrum. Re-examination by the roentgen ray was then done and a faintly defined fleck of barium was retained at the lesser curvature about 2 inches from the pyloric valve on the incisura angularis. The general appearance was that of a healing gastric ulcer with a very shallow crater. In concluding his report, the roentgenologist said, "I think it would be practically impossible to determine the lesion in the routine examination and the information gained from the gastroscopy probably made it possible for us to find this lesion."

Comment. This is a generous statement and indicates the good feeling and excellent cooperation between the two departments. In spite of the fact that gastroscopy first localized the lesion, the gastroscopic interpretation was erroneous whereas the roentgen diagnosis was correct.

CASE 15. L. B. (M.G.H., U No. 387907). On three occasions in four months the roentgen report was active or healing peptic ulcer grossly benign, located in the mid-portion of the lesser

curvature. This was well seen by gastroscopy as a deep triangular shaped ulcer (Fig. 5) on the lesser curvature of the angulus, about 2 by 0.5 by 0.5 cm. in size. The margins were reddened and slightly irregular, the base a rather dirty grayish pink. The mucosa surrounding the ulcer was markedly nodular and seemed somewhat rigid. Peristalsis was very inactive and did not pass normally over the ulcer. The examiner felt that the ulcer was probably malignant.

Comment. In this case all signs seemed to fail the gastroscopist. The irregular margins, the dirty base, nodular mucosa, rigid wall and abnormal peristalsis should have meant malignancy, but the roentgen report was correct in calling it benign. The pathological report was active benign gastric ulcer with chronic gastritis.

The other 2 cases in this group are quite similar to Case 15: G.H. (M.G.H. U No. 273526) being almost identical, and G.N.K. (M.G.H. U No. 317121) presenting a very similar problem. In the latter case four roentgen examinations were made, all showing one or two ulcers grossly benign. The gastroscopist examined this patient 5 times (the only case in my experience where there have been more gastroscopic than roentgen examinations) making a diagnosis of benign ulcer three times but then leaning toward malignancy because of the nodular mucosa surrounding the ulcers, distortion of peristalsis, failure to heal, short history and absence of free hydrochloric acid. The pathological report was gastric ulcer, marked acute and chronic gastritis. In many such cases there is no doubt surgery is indicated and the question of carrying out the correct procedure is of more importance than making the correct preoperative diagnosis. But in the long run, for the advancement of medicine we must strive for more and more accurate diagnosis by every method available.

There were also 4 cases in this group well seen by both roentgenologist and endoscopist, in which the latter was more accurate.

CASE 16. W. B. (M.G.H., U No. 171292).

Three roentgen examinations were made during a period of eleven months, each time revealing in the mid-portion of the lesser curvature an ulcer crater 1.0 cm. deep and 1.5 cm. across, with moderate thickening of the gastric wall. At the first examination it was considered grossly benign but with malignant change a distinct possibility. On the second and third



FIG. 5. Case 15. Gastroscopic appearance of ulcer grossly benign roentgenologically but thought to be malignant by gastroscopy because of the irregular margins and the nodular mucosa surrounding the ulcer. The base was described as a rather dirty gray. Moreover, peristalsis did not pass normally over the ulcer. The pathological report, however, was active, benign, gastric ulcer with chronic gastritis. In this case many of the usual signs of malignancy failed the gastroscopist.

examinations it appeared much the same but "should be considered malignant until proved otherwise." The gastroscopist reported an ulcer 1.0 by 1.5 by 0.5 cm. in the mid-portion of the lesser curvature, with a clean gray base and sharp smooth margins having the appearance of a benign gastric ulcer. "The gastroscopic findings point definitely toward a benign ulcer but microscopic malignancy cannot be positively excluded." The pathological report was gastric ulcer, subacute and chronic gastritis.

Comment. In this case the gastroscopist seemed more definitely in favor of a benign lesion.



FIG. 6. Case 18. First roentgen examination, antero-posterior view, no lesion demonstrable.

CASE 17. J.M.M. (M.G.H. U No. 16596). By roentgen examination the distal portion of the antrum was constantly narrowed and slightly irregular. On a second examination, there was a circular narrowing 1.5 cm. in length in the prepyloric area, probably due to a very small neoplasm. At a third examination the previous findings were confirmed—? old ulcer or very small tumor. As frequently happens, the roentgenologist suggested gastroscopy, which revealed a shallow oval ulceration about 1 inch from the pylorus on the lesser curvature—the ulcer had a clean white base and clear cut margins—probably a benign shallow ulcer. This was confirmed histopathologically after resection.

Comment. Although the prepyloric area is often difficult for the gastroscopist the description was very accurate in this case.

CASE 18. I.K. (B.M. U No. 44513). Roentgen report: "The stomach was difficult to examine because of its high transverse position and the thickness of the patient. As far as could be determined, however, there were no definite defects in the stomach (Fig. 6). Would like to

reexamine—" On the second examination there was found an area of ulceration of the anterior wall (Fig. 7) of the lower stomach, the appearance of which was grossly benign, but malignant changes could not be excluded. Gastroscopy demonstrated two gastric ulcers on the lesser curvature at the angulus. They were about 2 cm. apart, 4 mm. in diameter, 3 mm. deep, with sharp margins and clean gray base. The mucosa surrounding the ulcers was markedly red and edematous, but not nodular or verrucous and not suggestive of neoplasm. Close to the ulcers was a 3 mm. erosion and some fresh blood. Twelve days later gastroscopy was repeated showing one small benign healing gastric ulcer—nothing to suggest carcinoma. Roentgen examination two days after the second gastroscopy could no longer demonstrate an ulcer crater but reported "thickening of the mucosa in this region which could obscure a small crater. This area is extremely difficult to demonstrate by x-ray and I believe that gastroscopy is probably more accurate to determine

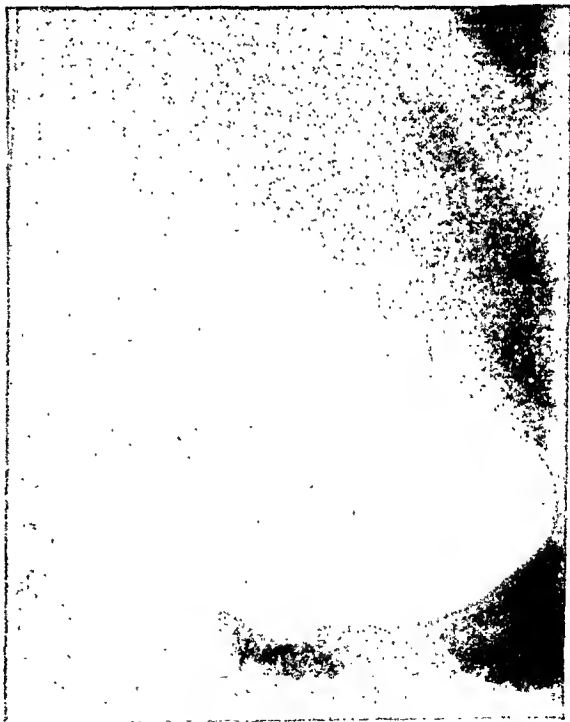


FIG. 7. Case 18. Later roentgen examination showing ulceration of anterior wall grossly benign, malignant changes not excluded. Gastroscopy in this case demonstrated two gastric ulcers on the lesser curvature at the angulus having a benign appearance. The pathologist reported two gastric ulcers with severe gastritis.

the question of regression." About two months later resection was done, and the pathologist reported two gastric ulcers with severe gastritis.

Comment. In this case the gastroscopist was able to demonstrate two ulcers and gastritis instead of only one ulcer. And the roentgenologist was frank in admitting the greater accuracy of gastroscopy.

CASE 19. J.M. (B.M. U No. 195485). A man, aged fifty-five, entered the hospital because of severe melena. Roentgen examination showed thickened gastric and duodenal mucosa with a definite deformity of the duodenum and what appeared to be a small ulcer crater on the posterior wall of the duodenum. Roentgenograms which were brought in by the patient showed a much larger crater in this area. Two weeks later reexamination of the esophagus, stomach and duodenum revealed no definite evidence of ulcer. There was practically no deformity of the duodenum. The small intestine was completely examined and showed no pathologic condition. There was a small hiatus hernia. No gastroscopy was done at that time but the patient was explored surgically and no pathologic condition found in the stomach or duodenum. Two weeks after operation gastroscopy revealed a very severe diffuse gastritis with erosions and active hemorrhage. The patient went home, was fairly well for four weeks and then suffered a massive hematemesis. After transfusions and jejunostomy for feeding a partial gastrectomy was successfully performed. The resected specimen showed a very small shallow ulcer on the lesser curvature of the stomach, no more than 3 mm. in diameter. It could not be palpated at the time of operation but it led directly into a large branch of the left gastric artery and it was from that source that the massive hemorrhage had come. There was no ulcer in the duodenum.

Comment. In this case although gastroscopy did not demonstrate the particular ulcer in question it did reveal the stomach as a probable source of the bleeding.

In reviewing these cases of proved gastric ulcer it is disappointing to find how many have not been seen by gastroscopy, but it is really not surprising that many prepyloric and lesser curvature antral ulcers are around the corner or otherwise invisible. Unfortunately, many ulcers are in these rel-

atively blind areas. It behooves us to improve our gastroscopes and our technique. Exclusive of mechanical difficulties, roentgen examination and gastroscopy seem to rate about equally, and each may contribute information of such value that neither examination can be omitted.

DUODENAL ULCER

Since it is impossible to see the duodenum by gastroscopy, the subject of duodenal ulcer is included chiefly because of the associated gastritis. The roentgenologist occasionally reports gastritis associated with duodenal ulcer but frequently does not mention it even if he finds thickened rugae and hypersecretion. The gastroscopist seldom examines the routine case of duodenal ulcer. If he does he will usually find some gastritis. The pathologist, if he examines the stomach histopathologically, always finds more or less gastritis in cases of duodenal ulcer; but unless he is making a special study he may not mention it.

Twenty-five cases of proved duodenal ulcer have had roentgenologic, gastroscopic and pathologic examination. Gastroscopic study is being done less frequently than formerly since it is indicated only under special circumstances. Only 6 of the 25 cases had gastroscopy since 1940; nineteen were done from 1933 to 1939 in an effort to evaluate the method. Pyloric obstruction, where the diagnosis is undetermined by roentgen examination, or in cases where carcinoma seems likely are frequent indications for gastroscopy; similarly unexplained gastrointestinal hemorrhage. Case 19 above is an example of a case thought to be bleeding from duodenal ulcer shown at gastroscopy to have severe gastritis with erosions and proved at operation to have bled from a very small gastric ulcer.

Occasionally, as in Case 3, there will be an eight year history of duodenal ulcer including surgery for a repair of perforation. In this case gastroscopy was very helpful in establishing the presence of a pathologic condition in the stomach in addition to the duodenal ulcer. It was believed to be prob-

ably malignant and was proved at operation to be carcinoma. The history of a proved duodenal ulcer was very misleading.

In duodenal ulcer are the symptoms due to the ulcer or to the associated gastritis? In at least 1 case (E.B., M.G.H. U No. 196632) the ulcer appeared to be healing at roentgen examination but the symptoms were getting worse, due apparently to a very active gastritis shown by gastroscopy. Also in hemorrhage from gastritis in the presence of duodenal ulcer I have raised the question^{1,2} as to whether the bleeding is coming mostly from the ulcer, which may be "old" or "healed" or "inactive" according to the roentgen reports, or from the gastritis which may be shown by gastroscopy to be severe with active bleeding.

JEJUNAL ULCER

Eight proved cases of jejunal ulcer have been examined by the roentgen ray and gastroscopy, in 3 of which the methods were equally good, in 2 equally incorrect and in 3 the roentgen ray was superior. There was no proved case of jejunal ulcer in which gastroscopy was superior.

In the 3 cases rated equally good, the jejunal ulcer was satisfactorily seen by the roentgenologist and also by the gastroscopist. In 1 case considered equally incorrect by both examinations, the stoma was well seen by both but no ulcer was visible. The pathologist, however—described shallow irregular ulcer crater at the site of the anastomosis probably too shallow to be seen roentgenologically and probably just around the corner for the gastroscopist. In the fifth case the jejunal ulcer was missed by both the roentgen ray and gastroscopy, the roentgen report describing a duodenal ulcer, normal gastroenterostomy stoma and question of carcinoma near the pylorus. The gastroscopist saw neither the pylorus nor the stoma but described a very nodular lesser curvature, which he thought was probably carcinoma.

The 3 cases in which roentgen examination was superior were due to the mechani-

cal difficulties of gastroscopy, viz. (a) stoma not seen at all; (b) stoma only partially seen; (c) multiple erosions seen on stoma but no ulcer visible.

Therefore, as in carcinoma and gastric ulcer, the mechanical difficulties of gastroscopy are the chief cause of its failure in the diagnosis of jejunal ulcer.

GASTRITIS

I believe roentgenologists, gastroscopists and pathologists would all agree that gastritis is the most common disease of the stomach. It occurs not only in association with ulcer and cancer but also as an independent entity. According to the Department of Radiology at the Massachusetts General Hospital, a diagnosis of gastritis can be made when there is thickening of the rugae and hypersecretion. Schatzki⁸ states that such rugae are wider, higher, and more rigid than normal folds; and one cannot make them disappear by pressure. Berg⁵ and Schatzki also stress the importance of increased gastric secretion and small round areas of diminished density which are due to particles of mucus. When these findings are present, roentgenologists have usually applied the term "hypertrophic gastritis." I believe this is unfortunate for it implies an ability on their part to differentiate the various types of gastritis—an ability which most roentgenologists admit does not exist. In my opinion, it would be safer under these conditions to say the findings suggest gastritis.

How often is such a diagnosis confirmed by the gastroscopist? A positive diagnosis of gastritis by an expert roentgenologist is usually but not always confirmed by gastroscopy. Occasionally after such a roentgen diagnosis the gastroscopist finds what he considers to be a normal stomach. Frequently he finds superficial gastritis or gastric atrophy instead of the hypertrophic variety. Superficial gastritis as seen gastroscopically corresponds to the acute gastritis described by the pathologist. In such cases the gastroscopist sees increased reddening, edema, and adherent secretion. The path-

ologist finds leukocytes filling the upper portions of the mucosa and a diminution of mucous vacuolization. Cases of superficial gastritis alone (i.e. without other gastric pathology) almost never come to surgery or to autopsy, but it has been possible to correlate the gastroscopic findings in superficial gastritis associated with ulcer or carcinoma with the pathological findings.

Benedict and Mallory⁴ carried out such a study in 51 resected specimens and found agreement in two-thirds of the cases of superficial gastritis, two-thirds of the cases of atrophic gastritis, and three-fourths of the cases of hypertrophic gastritis. The gastroscopist and pathologist agree in defining atrophic gastritis as atrophy of large areas of the mucous membrane, seen gastroscopically as a pale, thin mucosa with a network of easily visible blood vessels. Pathologically, the significant feature is the progressive diminution of the epithelial elements, with shortening of the glands and intestinal metaplasia. By "hypertrophic gastritis" the gastroscopist means a mucosa studded with verrucous elevations having a dull surface with few highlights and sometimes a beaded appearance to the rugae. The counterpart of the hypertrophic gastritis described by the gastroscopist appears to be the chronic gastritis which the pathologist recognizes by an exaggeration of the zone of plasma cell infiltration.

The cases studied by Benedict and Mallory were also reviewed from the roentgenologic standpoint by a member of the Department of Radiology who reported roentgen evidence of gastritis in almost every case. He could not differentiate the types of gastritis and made no attempt to do so. The criteria used were thickening of the folds and increased secretion. Pathologically, there is some evidence of gastritis in every case of peptic ulcer or gastric tumor. Therefore one might question the importance of these studies. I believe the significance lies in thus proving the ability of the roentgenologist and gastroscopist to diagnose gastritis not only in association with ulcer or cancer but also as an independent

entity, for the diagnostic criteria are the same.

The unquestioned superiority of gastroscopy in differentiating the various types of gastritis is important, for gastritis besides being the most common disease of the stomach is undoubtedly the cause of symptoms. Superficial or acute gastritis is seen in alcoholism, seasickness, airsickness, dietary indiscretion, infectious disease, and in so-called indigestion. It is usually of comparatively short duration and probably 90 per cent of such patients do not need roentgenologic or gastroscopic examination. If symptoms persist, however, it is important from the standpoint of treatment and prognosis to determine whether there is serious gastric disease, acute or chronic gastritis or gastric neurosis. In a series of 1,300 cases examined gastroscopically by Benedict,³ chronic or hypertrophic gastritis without other gastric or duodenal pathology was found in 117 cases (9 per cent). Pain, vomiting, bleeding, sour eructations and heart burn are frequent symptoms. Pain may be similar to ulcer pain. Hemorrhage from gastritis deserves special mention for very severe hemorrhage can occur from gastritis alone. Some hemorrhage occurred in 42 per cent of the 117 cases. A roentgen diagnosis of gastritis was mentioned in only one-third of the 117 cases. Atrophic gastritis or gastric atrophy may be a late stage of an inflammatory process or may be the result of a deficiency disease such as pernicious anemia, sprue, pellagra, and so forth. It is found commonly with carcinoma, rarely with ulcer. The diagnosis is important, for liver therapy may be specific (Jones, Benedict and Hampton).⁶ It is impossible to correlate the thickened folds and increased secretion sometimes reported by roentgen ray with the thin mucosa, absence of folds and lack of secretion seen at gastroscopy. Undoubtedly the gastroscopic diagnosis is more accurate.

Sixteen cases proved pathologically to have only gastritis have been explored surgically, 12 because of the possibility of cancer (Fig. 8, 9 and 10), 3 because of



FIG. 8. W.M. (M.G.H. U No. 409299). The roentgenogram shows polypoid masses in the fundus thought to be polypoid tumor. Gastroscopy showed severe gastritis with ulcers. The pathological report after resection was multiple peptic ulcers, erosions, acute and chronic gastritis.

hemorrhage, and 1 because of the possibility of jejunal ulcer. Five times the two methods of examination seemed equally poor, nine times gastroscopy was considered superior and twice roentgen examination seemed better.

In the 5 cases rated equally poor, 3 were thought to be cancer by both methods; 1 was spasm of the pylorus by roentgen examination, carcinoma of the greater curvature by gastroscopy; and the fifth case was thought to be a large carcinoma of the greater curvature by the roentgen ray, unsatisfactory examination (due to spasm) by gastroscopy.

In 9 cases gastroscopy seemed more accurate than the roentgen examination. In 2 of these (B.D., M.G.H. U No. 334863; A.J., M.G.H. U No. 186668), the roentgenologist reported prepyloric ulcer which

was not substantiated pathologically after resection. In both these cases the gastroscopist saw the pylorus and the prepyloric area and could see no ulcer. The gastritis reported by gastroscopy in both cases was confirmed by the pathologist. In a third case (A.R., M.G.H. U No. 300945) the roentgenologist suspected carcinoma or lymphoma of the lesser curvature near the cardia (Fig. 11). In the same area the gastroscopist reported very severe hypertrophic gastritis, which was confirmed by open tube gastroscopic biopsy and also later by exploratory laparotomy and gastrotomy. In 2 other cases (D.V., M.G.H. U No. 57777; E.C.M., M.G.H. U No. 9439), the question of jejunal ulcer or duodenal ulcer was raised by roentgen examination but not found at operation. While the gastroscopist could not exclude these lesions, he did find gastritis which was con-



FIG. 9. J.M. (M.G.H. U No. 355822). Compare with Figure 8. Polypoid lesions of the fundus thought to be due to gastritis. Gastroscopy was reported gastritis. Later resection proved to be carcinoma.



FIG. 10. G.L. (P.M.H. U No. 43-595). Ulcerating carcinoma of antrum readily demonstrated by gastroscopy as shown above but confused with gastritis at the roentgen examination.



FIG. 11. A.R. (M.G.H. U No. 300945). Third case of the 9 cases of gastritis in which gastroscopy seemed more accurate than the roentgen ray. Roentgen appearance is suspicious of carcinoma or lymphoma of the lesser curvature and near the



FIG. 12. E.D. (M.G.H. U No. 29583). Sixth case of the 9 cases in which gastroscopy seemed more accurate than the roentgen ray. In this case the roentgenologist was uncertain as to whether he was dealing with foreign bodies or polyps in the stomach with a possible pyloric ulcer or carcinoma. The gastroscopist reported a prune stone and a plum stone with gastritis, as shown in this illustration. Operation confirmed these findings. (Reproduced through the courtesy of Oxford Medicine.)



FIG. 13. C.H. (P.H. U No. 1312). Eighth case of the 9 cases in which gastroscopy seemed more accurate than the roentgen ray. In this case the roentgen report was gastritis, but gastroscopy was far more specific in describing active bleeding from erosions and superficial ulcerations in a severe gastritis. This was confirmed at operation. (Reproduced through the courtesy of Oxford Medicine.)

cardia. In the same area, the gastroscopist reported very severe hypertrophic gastritis, confirmed later by open tube gastroscopic biopsy and exploratory laparotomy.

firmed by the pathologist. In a sixth case, (E.D., M.G.H. U No. 29583) the roentgenologist was uncertain as to whether he was dealing with foreign bodies or polyps in the stomach, with a possible pyloric ulcer or carcinoma; the gastroscopist reported a prune stone and a plum stone with gastritis (Fig. 12). Since the stones failed to pass the pylorus, operation was performed confirming these findings and showing no ulcer or carcinoma. In the seventh case (M.M., M.G.H. U No. 318232) a large carcinoma of the greater curvature was demonstrated roentgenologically but only hypertrophic gastritis was reported by gastroscopy; no carcinoma was found on exploration. The eighth (Fig. 13) and ninth cases (C.H., P.H. U No. 1312; J.E.K., M. G.H. U No. 30620) concerned hemorrhage from postoperative gastritis, in which the roentgen report was gastritis but gastroscopy was far more specific in describing active bleeding from erosions and superficial ulcerations in a severe gastritis.

In 2 cases in this group it seems fair to rate the roentgen ray better than gastroscopy. The first was E.W. (P.H. U No. 129080) in which case the roentgen finding was a localized area of polypoid gastritis, ulcerating neoplasm possible but unlikely; by gastroscopy, however, it was felt the lesion was atypical but consistent with infiltrating neoplasm. A subtotal resection was done, the pathological report being chronic gastritis. The second case (J.S., M. G.H. U No. 283404) was not much credit to either method of examination, the roentgenologist reporting on three examinations old duodenal ulcer, ? ulcer in pylorus, shallow ulcer lesser curvature side of pylorus, small flat ulcer in the immediate prepyloric area, possibly malignant. Gastroscopy was satisfactory and was entirely negative, with no evidence of gastritis. The surgeon did a subtotal resection finding no ulcer. The pathologist found no ulcer or neoplasm, but reported acute and chronic gastritis. On reviewing the roentgenograms the radiologist reported thickening of the folds and

increased secretion, indicative of gastritis in his opinion.

It is evident, then, that gastritis may be found by the pathologist when it cannot be detected by the gastroscopist. I know of 7 cases of duodenal or gastric ulcer in which the gastroscopist specifically stated he could see no evidence of gastritis, but some gastritis was found by the pathologist. This is more apt to be true in the antrum than in the body of the stomach, and is best explained probably by the fact that the gastroscopic view is less satisfactory in the antrum. The occasional failure of gastroscopy to diagnose gastritis is probably of no great significance.

In 12 of the 16 cases reported above, the question of a malignant condition was raised. Under such circumstances the difficulty has always been that once either the roentgenologist or the gastroscopist raises the question of neoplasm neither one is willing to exclude it and the patient must then be explored. Even with suitable equipment for endoscopic gastric biopsy, which we do not now possess, positive exclusion of malignancy may still be doubtful owing to the possibility of obtaining tissue from the wrong area.

In spite of the occasional failure of gastroscopy in the diagnosis of gastritis, we have a great deal of pathological evidence of its accuracy and specificity in proved cases of gastritis occurring with or without other gastric disease. Such accurate and specific correlation between roentgenological and pathological findings in gastritis is lacking.

BENIGN TUMOR

Seven proved benign tumors were studied, of which 3 were described pathologically as adenomatous polyps, 1 polyp, 1 polyposis, 1 neurofibroma, and 1 leiomyoma. On three occasions roentgen examination and gastroscopy seemed about equal twice the roentgen ray was better, and twice gastroscopy was better.

Three times roentgen examination and gastroscopy were about equally good,

doubtful or incorrect: once (I.S.C., B. M. U No. 160436) both methods were roughly correct in describing multiple polyps, ? malignancy; a second time (A.A., M.G.H., U No. 187961) both doubtful in describing a large pedunculated tumor mass in the antrum probably malignant; and in the third case (E.C.T., P.H., U No 33749) both incorrect as a 1 cm. leiomyoma of the body of the stomach was thought to be scirrhus carcinoma of the pylorus at roent-

copy. The pathological report was benign adenomatous polyp on the greater curvature 7 cm. from the pylorus. In these 2 cases the superiority of the roentgen examination



FIG. 14. E.S. (M.G.H. U No. 6073). Gastroscopic appearance of long smooth polypoid lesion of antrum probably benign, thought to be carcinoma by roentgen examination. This proved to be a long finger-like benign polyp. (Reproduced through the courtesy of the *New England Journal of Medicine*.)

gen examination and was not seen at all by gastroscopy.

Roentgen examination was definitely superior in 2 cases: (1) (A.I.B., M.G.H., U No. 218777) reporting very accurately an oval lesion on the greater curvature of the antrum, possibly leiomyoma or early carcinoma. This lesion proved to be an adenomatous polyp and was not seen at all by gastroscopy; (2) (M.K., P.H., U No. 206463) roentgen ray reported one or more polyps in the lower stomach on the greater curvature but these were not visible by gastros-



FIG. 15. J.E.S. (P.H. U No. 270243). Gastroscopic appearance of a submucosal tumor thought to be benign by gastroscopy. The pathological report was neurofibroma. Roentgen examination at another institution had reported this as carcinoma (see Fig. 16). (Reproduced through the courtesy of Oxford Medicine.)

was due to the mechanical difficulties of gastroscopy.

Twice gastroscopy was more accurate than the roentgen examination: once (E.S. M.G.H., U No. 6073) describing a long smooth polypoid lesion (Fig. 14) of the antrum probably benign, whereas it was thought to be carcinoma roentgenologically. This proved to be a long finger-like benign polyp. In the other case (J.E.S., P.H., U No. 270243) the roentgen examination in another city described a carcinoma of the antrum, gastroscopy reported a submucosal tumor with a small ulceration on it (Fig. 15). After the gastroscopy another roentgen examination revealed an intramural tumor (Fig. 16). The pathological report was neurofibroma.

It is evident from these 7 cases of benign tumor that the chances of error are fairly large and that we come closer to the correct diagnosis if both methods of examination are used, especially when they are used in close cooperation with each other.

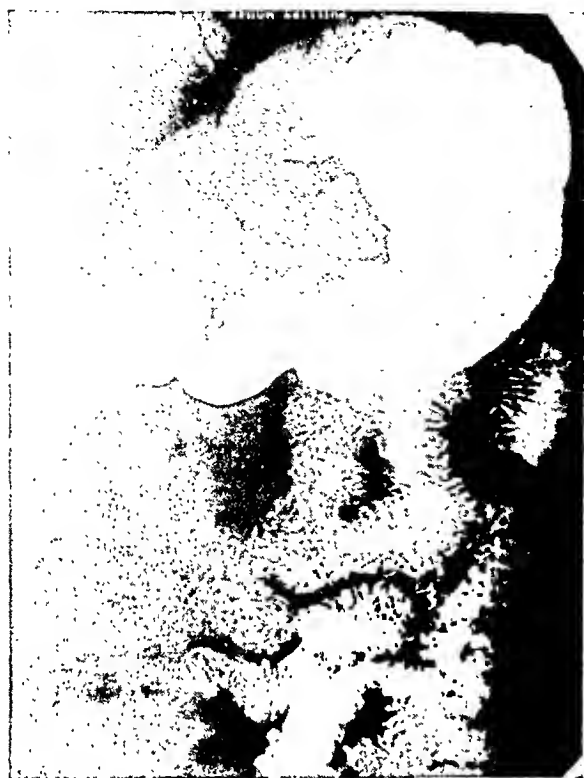


FIG. 16. Roentgen appearance of lesion shown in Figure 15. This roentgenogram was taken following gastroscopy and confirmed the gastroscopist's opinion. The first roentgen report in another institution had been carcinoma.

LYMPHOMA

Five cases of proved lymphoma have been studied roentgenologically and by gastroscopy. In 3 cases the lesion seemed to be quite typical of carcinoma by both methods of examination. In the fourth case (N.I., M.G.H., U No. 314994) the roentgenologist reported a lesser curvature lesion consistent with a 1 inch saddle ulcer associated with an unusual type of gastritis. This happened to be the first case in the United States examined by the flexible gastroscope (April 6, 1933), and no definite conclusions were reached. The fifth case (P.B., M.G.H., U No. 289112) was the only one in which lymphoma was mentioned by either method of examination. During a seven month period the roentgenologist studied this patient eight times. On the first examination he described a large ulcer at the posterior wall of the fundus, possibly benign or malignant, lym-

phoma to be considered (Fig. 17). On seven subsequent examinations he described marked swelling of the folds on four occasions, with no ulcers twice and two or three grossly benign ulcers at other times. The question of malignant ulcer of lymphoma was mentioned only on the first examination. During the same period the gastroscopist made six examinations concluding successively as follows: (1) multiple gastric ulcers and erosions with hemorrhage; severe superficial and hypertrophic gastritis (Fig. 18); neoplasm not excluded; advise House admission; (2) very suspicious of carcinoma; exploration should be done unless the Department of Radiology excludes malignancy; (3) very severe hypertrophic gastritis, probably not malignant; (4) extremely severe hypertrophic gastritis with multiple gastric ulcers on the greater curva-



FIG. 17. P.B. (M.G.H. U No. 289112). Roentgen appearance showed very thick folds in the fundus. Lymphoma was mentioned as a possibility on one of eight examinations. Pathological report malignant lymphoma (see Fig. 18).

ture—neoplasm a possibility; (5) unsatisfactory due to spasm and secretions—"because of repeated occurrences of ulceration in various parts of the stomach, I believe radical resection will be inevitable;" (6) erosions and clots of blood on greater curvature but no ulcer demonstrable—very severe hypertrophic gastritis with erosion and hemorrhage. "I still believe that partial gastric resection will be inevitable." The pathology report was malignant lymphoma lymphocytic type, with peptic ulceration.

In considering these 5 cases of lymphoma it seems that at the present time the best we can hope for is to suspect it occasionally as in the last case. The roentgenologist based his suspicion on unusually thick rugae which he said were "possibly due to hypertrophy but there was a possibility also that the thickened rugae may represent lymphomatous infiltration." On seven

subsequent examinations, however, he mentioned neither carcinoma nor lymphoma. In five out of six gastroscopies the question of malignancy or surgery was raised.

The diagnostic criteria to look for in lymphoma may be unusually thick rugae, very marked cobblestone mucosa, multiple erosions and ulcerations in various parts of

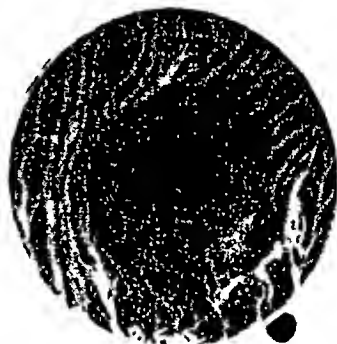


FIG. 19. E.L. (M.G.H. U No. 279061). In this case of proved neurogenic fibrosarcoma, the roentgenologist reported a 7 by 5 cm. mass arising from a broad base—first choice leiomyoma, much less likely carcinoma. The gastroscopist described a smooth lesion as seen in this illustration with no visible ulceration—probably benign leiomyoma or neurofibroma. Neither method of examination made the correct diagnosis.



FIG. 18. P.B. (M.G.H. U No. 289112). Gastroscopy demonstrated multiple gastric ulcers and erosions with hemorrhage. The marked cobblestone appearance led to a gastroscopic diagnosis of hypertrophic gastritis. Neoplasm, however, was suspected but lymphoma was not specifically mentioned. The pathological report was malignant lymphoma, lymphocytic type, with peptic ulcerations. (Reproduced through the courtesy of *Surgery, Gynecology & Obstetrics*.)

the stomach at different times, with or without rigidity or a tumor mass. With further experience in both roentgen examination and gastroscopy, correct diagnosis may be possible.

SARCOMA

Only 2 cases fall in this group, both of which were proved histopathologically to be neurogenic fibrosarcoma. In the first case (G.W.W., M.G.H. U No. 328837), the roentgenologist demonstrated a constant 3 cm. concave pressure defect on the lesser curvature near the angularis, very suggestive of a mural tumor. Unfortunately, this tumor was not seen by gastroscopy (another very early case in the career of the gastroscopist, April 29, 1933). In the other

case (E.L., M.G.H., U No. 279061), the roentgenologist reported a 7 by 5 cm. mass arising from a broad base of the lesser curvature and posterior wall of the fundus of the stomach (Fig. 19). The surface was rather smooth with one slight lobulation and one deep ulceration: first choice, leiomyoma; second choice, much less likely carcinoma. The gastroscopist described a smooth rounded submucosal tumor with



FIG. 20. E.S. (P.H. U No. 296104). Gastroscopic appearance of smooth rounded mass projecting from the lesser curvature and posterior wall of the antrum thought to be a benign tumor by gastroscopy but proved at operation to be carcinoma of the pancreas invading the wall of the stomach submucosally (see Fig. 21).

no visible ulceration—probably benign leiomyoma or neurofibroma.

Since the benign neurofibroma previously described was also slightly ulcerated it would seem that there may be no way of differentiating a benign from a malignant intramural tumor. In the malignant case, however, the tumor was larger and the ulceration deeper. Further roentgenologic and gastroscopic experience will be important.

METASTATIC CARCINOMA

In 3 cases a carcinoma of the pancreas

was proved at operation to have invaded the wall of the stomach. In the first case (M.B., M.G.H. U No. 270419), the roentgenologist found definite rigidity along the lesser curvature of the body of the stomach and made a diagnosis of a malignant lesion, probably carcinoma, involving a large portion of the body of the stomach. On gastroscopy the instrument met complete obstruction about 2 cm. inside the cardia; this obstruction was thought to be probably due to neoplasm but no satisfactory view was obtained. In the second case (D.J.McC., M.G.H. U No. 332957), roentgen examination showed marked deformity of the antrum, pylorus and duodenal loop probably from extrinsic involvement, but carcinoma of the pancreas could not be diagnosed. Gastroscopy demonstrated normal mucosa and rugae throughout. In the third case (E.S. P.H., U No. 396104), several preliminary roentgen examinations at an outside hospital demonstrated a normal stomach. Gastroscopy, however, revealed a constant smooth mass about 3-4 cm. in diameter covered with normal mucosa, projecting from the lesser curvature and posterior wall of the antrum (Fig. 20). It was not ulcerated and peristalsis appeared to pass smoothly over it. It was thought to be a benign tumor—neurofibroma or leiomyoma. Roentgen examination later confirmed this filling defect without ulceration and concurred in the opinion that it was likely to be a neurofibroma (Fig. 21).

In none of these cases did either method of examination make the correct diagnosis, yet each contributed something in each case. In the first case, both methods revealed an abnormality, the roentgen examination being more specific but incorrect nevertheless. In the second case, the roentgen ray was more valuable, demonstrating a lesion that was probably extrinsic, gastroscopy confirming a normal gastric mucosa. In the third case the gastroscopist first demonstrated a gastric lesion, in the face of negative roentgen findings, but his conclusions as to the diagnosis were incorrect.

NORMAL STOMACH

Four patients in this series have been explored because of the possibility of carcinoma but no gastric lesion was found.

CASE 20. R.B. (M.G.H. U No. 53367). Five roentgen examinations were done over a period of six months, the first being inconclusive but suggesting a deep ulcer crater in a carcinoma, the second, third and fourth failing to demonstrate a carcinoma, but the fifth showing a "large irregular filling defect at fundus of stomach." Two gastroscopies were done and showed gastritis but no tumor. Surgical exploration revealed no gastric abnormality.

Comment. The stomach was not opened and a small soft tumor or gastritis might therefore have been overlooked, but roentgen examination nine months later was negative for tumor though it did show some increase in the size of the rugae.

CASE 21. W.D. (M.G.H. U No. 37616). The roentgenologist studied this patient on three successive days, demonstrating marked swelling and slight irregularity of the rugae in the upper half of the stomach, more likely a diffusely growing neoplasm than a localized hypertrophic gastritis. The gastroscopist demonstrated superficial gastritis and an irregular, slightly elevated area about 1.5 inches below the cardia, near which there was a papillary nodule, consistent with early carcinoma. Exploratory laparotomy with gastrotomy revealed no evidence of carcinoma. Biopsy of the gastric mucosa was reported normal stomach.

Comment. Both examiners suspected a carcinoma which was not found at operation. Histopathologically there was not even any gastritis, though the house officer assisting at the operation reported "considerable hypertrophic gastritis." Naturally one would question such an observation and one would also wonder from exactly what area the biopsy was taken.

CASE 22. M.O. (M.G.H., U No. 289057). Several roentgenograms and one gastroscopy were negative in this case. Exploration was done, however, because of a previous laparotomy at another hospital three months before admission, at which time, a small, fairly well circumscribed mass was found on the anterior



FIG. 21. Roentgen appearance of lesion shown in Figure 20. The first roentgen examination made in another city had been reported as normal stomach. Roentgen examination after gastroscopy confirmed the filling defect without ulceration and the roentgenologist felt that it was probably a neurofibroma. In retrospect, however, the roentgenologist felt that the diagnosis of carcinoma of the head of the pancreas could have been made because of the extrinsic pressure on the second portion of the duodenum as shown in this illustration.

wall of the stomach near the pylorus. Biopsy of this mass at that time was reported as a slowly growing adenocarcinoma. At the second exploration there was a rather firm tumor adjacent to the lesser curvature and posterior wall of the stomach and probably arising from the stomach. Resection was performed, the pathology report being ectopic pancreas in duodenum.

Comment. The roentgenologist and gastroscopist were both correct in reporting no disease of the stomach.

CASE 23. J.O. (P.M.H. U No. 41-100). In this case two roentgen examinations were reported as showing an irregular gastric outline near the cardiac orifice for a distance of about 4 cm. and a diagnosis of carcinoma involving the cardiac orifice was made. Gastroscopy was

done by the straight rigid open tube method and no tumor was visible at the cardia or in the upper stomach. A biopsy was obtained which was reported as normal gastric mucosa. In order to be absolutely certain, the patient was explored surgically by the transthoracic route and no tumor was found. Roentgen examination two and a half years later showed only slight cardiospasm and normal stomach.

In the above 4 cases the roentgen examination and gastroscopy were equally correct in demonstrating no disease of the stomach in Case 22, and about equally incorrect in suspecting a non-existent carcinoma in Case 21. In Cases 20 and 23 the roentgenologist diagnosed carcinoma which was in fact not present, and which had been ruled out as far as possible by gastroscopy. In these 2 cases, therefore, the gastroscopist was correct and the roentgenologist incorrect, but, as previously stated, the exclusion of a gastric neoplasm by any method cannot be absolutely positive.

DISCUSSION

It seems fairly obvious that both the roentgen examination and gastroscopy occupy a very important place in the diagnosis of gastric disease. It has already been admitted that evaluation of the relative merits of the two methods is somewhat arbitrary. It is also unfair because they are so different and work so well to supplement each other. Theoretically such a comparison should not be attempted but practically it is helpful to know where we stand and in what types of gastric disease we can expect the best results from each method. Some of the gastroscopic errors made ten years ago were due to inexperience and would not be made today. There has also been an improvement in roentgen examination of the stomach, notably by the use of the relief technique and spot roentgenograms. It is quite clear from the above analysis of cases that by the judicious use of both methods greater diagnostic accuracy can be obtained than by the use of either method alone.

Gastroscopy is indicated in cases of gastric pathology where the diagnosis is in doubt. Patients with hematemesis or melena may have negative roentgen findings; gastroscopy may show the cause of the bleeding to be a severe gastritis with erosions and superficial ulcerations. Serious hemorrhage may come from such a gastritis in the absence of other pathologic condition. Similarly patients with an otherwise unexplained anemia may be found by gastroscopy to have gastric pathology. Lesions of the lesser curvature may be benign or malignant; the differential diagnosis may be impossible by roentgen examination. In such cases the gastroscopist may be able to make a positive diagnosis. When the question arises as to medical or surgical treatment in a given case, gastroscopic examination may definitely swing the balance one way or the other. Cases of pyloric obstruction or pylorospasm may be impossible to diagnose roentgenologically; such cases should be studied by gastroscopy, for in some of them the gastroscopic diagnosis is comparatively easy. So it goes, one method supplementing the other. Cases difficult to diagnose by gastroscopy may be easy roentgenologically, and vice versa. Lesions high up on the greater curvature may be hard to palpate and visualize by the roentgen ray; such cases should have gastroscopy, for usually this area is easy to see with the gastroscope. On the other hand, small lesions close to the pylorus, on the lesser curvature of the antrum, high on the lesser curvature of the body, and high in the fundus may be impossible to see by gastroscopy but easy to see roentgenologically. The differential diagnosis of hypertrophic gastritis and carcinoma may be impossible, but gastroscopy should be done as it may be quite definite in determining the course to pursue. Finally, many patients have gastrointestinal symptoms with repeatedly negative roentgen findings; such patients may be erroneously classified as gastric neurotics until gastroscopy reveals gastritis.

Excluding duodenal ulcer we are dealing in this report with 220 cases of gastric disease in which there is a positive pathological diagnosis. Analysis of these cases shows the roentgen examination and gastroscopy equally correct in 88 (40 per cent); equally doubtful in 14 (6 per cent); equally incorrect in 17 (8 per cent); roentgen examination superior in 63 (29 per cent); gastroscopy superior in 38 (17 per cent). In 50 cases (21 per cent) the failure of gastroscopy was attributable to the mechanical difficulties of instrumentation, with consequent inability to properly visualize certain parts of the stomach. If these could be overcome the superiority of the roentgen examination would be reduced from 63 cases to 13 (6 per cent) as against the 38 cases (17 per cent) in which gastroscopy was more accurate. This would appear to indicate that if the gastroscopist obtains a satisfactory view of the lesion he has a better chance than the roentgenologist of making a correct diagnosis. The finding of 31 cases (14 per cent) where both methods were equally doubtful or incorrect is somewhat disturbing and indicates that our diagnostic methods leave much to be desired. Fortunately, clinical judgment has not been entirely forgotten in these days of scientific advancement and the wise physician will assemble the available data and usually arrive at the proper medical course or surgical procedure.

CONCLUSIONS

Two hundred and forty-five cases of proved carcinoma, gastric ulcer, duodenal ulcer, jejunal ulcer, gastritis, benign tumor, lymphoma, sarcoma, metastatic carcinoma of the stomach wall, and normal stomach have been studied in an attempt to correlate the roentgen and gastroscopic findings in each case with the known pathologic diagnosis.

Although it is unfair to compare the roentgen examination with gastroscopy, since the latter supplements the former and is in no way competitive, it can be stated

that in certain instances the roentgen examination appears to be superior to gastroscopy, and in other cases gastroscopy appears to be superior to the roentgen ray.

The roentgen examination and gastroscopy were about equal in 54 per cent of the cases, roentgen examination was considered superior in 29 per cent, gastroscopy superior in 17 per cent.

The chief causes of failure in gastroscopy are mechanical. If mechanical difficulties could be eliminated the number of cases in which the roentgen examination appears to be superior to gastroscopy would be reduced to 13 (6 per cent) as against the 38 cases (17 per cent) in which gastroscopy seemed more accurate.

From this analysis it appears that if the gastroscopist can get a satisfactory view of the lesion his chances of reaching a correct diagnosis are greater than those of the roentgenologist.

Gastroscopists must therefore strive to bring about improvements in the gastroscope so that blind areas may be eliminated and biopsies easily taken.

Greater diagnostic accuracy is attainable when both methods are used cooperatively than when either method is used alone.

The proper procedure for the patient is all-important and to this end there must be close cooperation between the clinician, roentgenologist, gastroscopist and pathologist.

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SPONDYLOLISTHESIS

CRITERIA FOR MORE ACCURATE DIAGNOSIS OF TRUE ANTERIOR SLIP OF THE INVOLVED VERTEBRAL SEGMENT*

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SPONDYLOLISTHESIS is a well known and fairly common disorder, which has assumed increasing importance in recent years in connection with the care and disposition of military and industrial personnel, especially of those claiming disability from lumbosacral backache. The incidence in the ordinary population is quite low (perhaps 5 per cent of adults), but in large general hospitals, especially those handling Army and Naval personnel, its incidence is comparatively high (as much as 10 per cent of "low back" cases referred for roentgen examination).

The recognition of advanced spondylolisthesis in middle aged and elderly persons, especially women, is relatively simple, and the diagnosis may often be made clinically. Indeed, the first reported cases were discovered as obstetrical problems (shortened true conjugates).¹⁶ Moderate and even slight degrees of slip may sometimes be correctly diagnosed by the alert orthopedist. However, the diagnosis of minimal degrees of spondylolisthesis in early cases is usually difficult, and often complicated by the fact that, while the posterior margin of the fifth lumbar body may appear to be displaced forward, its anterior margin may be found in normal alignment with the margins of the adjacent bodies. This may be due to the presence of a congenitally foreshortened fifth lumbar body, and the problem then arises as to which surface of this body should be regarded as the criterion for estimating displacement, the anterior or the posterior surface. It is in an attempt to clarify this point that the present study was undertaken.

TERMINOLOGY

Spondylolisthesis (*spondylos*, a vertebra;

olisthesis, to slip) is defined as anterior displacement of a vertebral body with solution of continuity of its posterior arch. Strictly speaking, the displacement usually involves the body plus its transverse processes, pedicles, superior articular processes, and adjacent ventral portions of the laminae. The solution of continuity in the arch is nearly always bilateral and usually consists of *slender fissures in the interarticular portions* of the neural arch. This is the common type of spondylolisthesis, and may be termed true spondylolisthesis. It can occur almost anywhere in the spine but is most common in the lower lumbar area, involving usually the fifth or last lumbar segment.

There are various other types of displacement and change in this area which do not fit strictly into the classification of true spondylolisthesis, but which are sometimes confused with it. These include:

(a) *Anterior dislocation of a lower lumbar vertebra*, a fairly rare condition associated usually with fractures of the articular processes of this or the adjacent segments, but sometimes associated with simple luxation of the posterior articulations of the involved segment. These fractures or dislocations may be on a traumatic or pathologic basis (inflammatory disease, metastatic neoplasm, degenerative osteoarthritis with erosion of facets, etc.).

(b) *Elongation of a lower lumbar body* (localized platyspondyly). The body is elongated in the sagittal plane and its anterior (or posterior) margin projects in front of (or behind) the normal zone, but the neural arch is not defective. The elongation may be congenital or acquired.

(c) *Foreshortening of a lower lumbar body* (localized brachyspondyly). The body is foreshortened in the sagittal plane; its an-

* The opinions and views set forth in this article are those of the writers, and are not to be considered as reflecting the policies of the Navy Department.

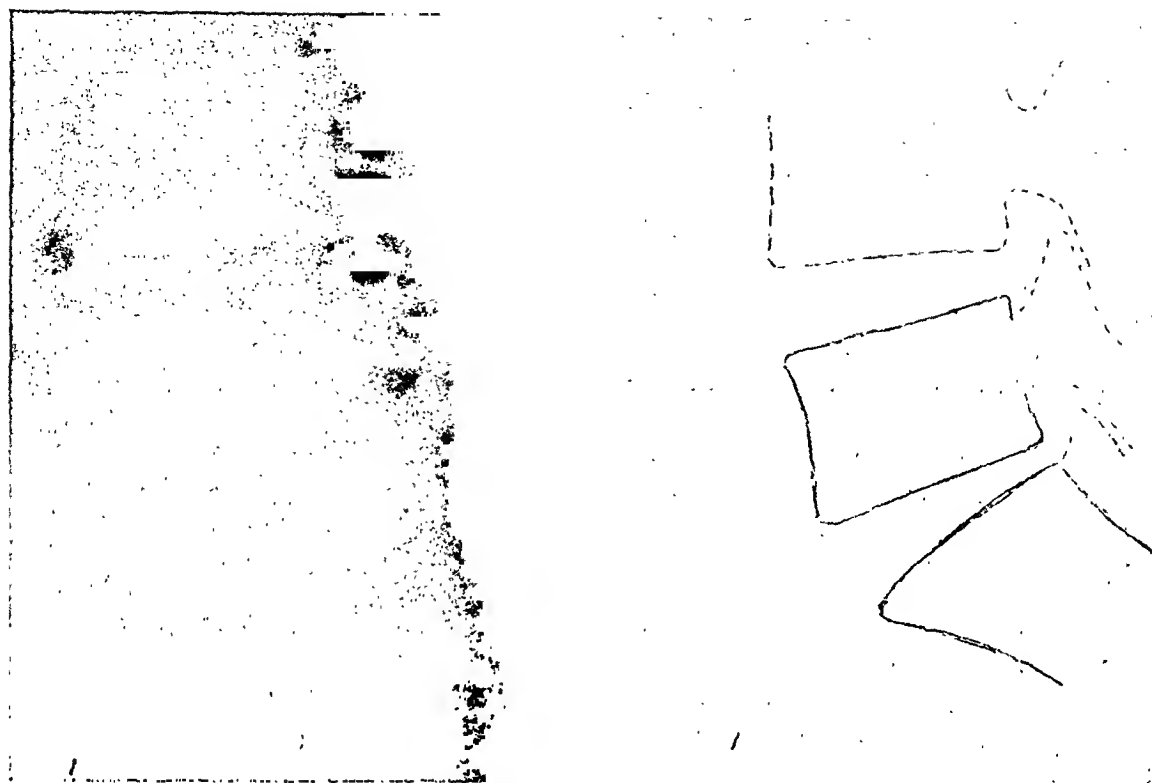


FIG. 1. Normal "rectangular" type of fifth lumbar body. When the body is of this shape, the detection of true slip is much simpler than when it is caudally foreshortened (hatchet shaped) or otherwise unusual in shape. The term "rectangular" is a relative one, since when measured, most fifth lumbar bodies that appear to be rectangular in lateral projections are found to be slightly wedge shaped, the vertical dimensions of their posterior surfaces being from 2 to 8 mm. less than the vertical dimensions of their anterior surfaces.

terior margin may be in normal alignment with those of its fellows, but its posterior margin is from 1 to several millimeters ventral to that of the subjacent segment, and sometimes ventral to that of the superjacent segment also. In addition to being foreshortened, these bodies are often wedge or hatchet shaped. There may or may not be interarticular defects in the neural arch of the involved segment. When there are, these cases are often erroneously labeled "spondylolisthesis grade I," when in fact, no true slip has occurred. Once labeled such, these cases tend to become progressively symptomatic. They or their attendant family physician, seeing the word spondylolisthesis applied to their simple anatomic lesion, may conjure up the clinical description of the disorder seen in some orthopedic textbooks:

A dimple appears in the back at the lumbo-

sacral junction; the umbilicus seems very near the symphysis, and the arms of the individual appear to be extra long. This displacement may lead to severe pain in the back, sacro-iliac regions, thighs and feet. The roentgenograms may show in the lateral view the body of the fifth lumbar rotated well down in front of the sacrum.*

In addition to "true" and "false" spondylolisthesis, there are two other terms used somewhat loosely for conditions in this area. These are "prespondylolisthesis" and "reverse spondylolisthesis."

Prespondylolisthesis is mentioned only to be condemned. It is a fearsome word, philologically and psychologically, applied to a condition in which there are interarticular defects in the neural arch of a vertebral

* Speed, Kellogg. A Text-Book of Fractures and Dislocations Covering Their Pathology, Diagnosis and Treatment. Fourth edition. Lea & Febiger, Philadelphia, 1942, p. 232.

segment with no forward displacement of the anterior portion of that segment. The term is unwise because it implies that subsequent slipping of the body is almost inevitable, and it is confused in the minds of many physicians and patients with the true entity. It may unfairly restrict or prevent proper employment of an individual, and result in considerable mental as well as economic hardship to him and his family. Some authors use the word "spondylolysis" for the condition. We believe that the term "neural arch defects without visible slip of body" is clearer and preferable.

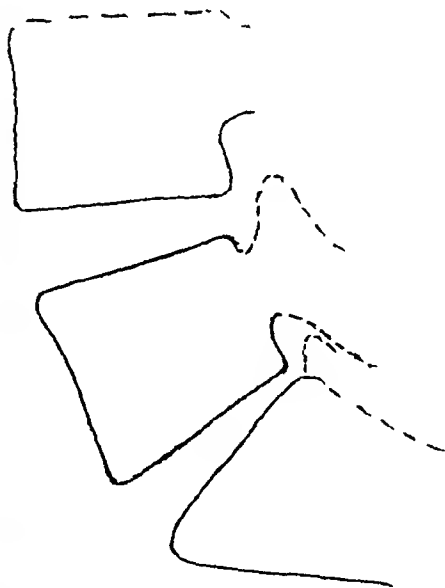
Reverse spondylolisthesis is also mentioned to be condemned. The complex term is applied to a condition in which a vertebral body lies or appears to lie on a plane dorsal to that of its fellows. It is rarely or never due to interarticular defects in the neural arch, nor associated with true to-and-fro slipping. If actually present, it is usually a fixed condition, secondary either to anomalous development of the articular

processes or bodies, or to bizarre disease or trauma of the same. A foreshortened first sacral body may cause the last lumbar segment to have this appearance.

ETIOLOGY

The cause of the forward slipping of the involved vertebral segment (along with the superjacent spinal column) is presumed to be the normal stress of weight of the body, in some instances combined with occupational strains, trauma, weakening of muscles and ligaments from age or disease, and softening of some of these structures from pregnancy—all in the presence of a vertebral segment with a defective neural arch.

The cause of the defects is still unknown, in the majority of instances. It was first believed that they were *traumatic* in origin.^{8,16} Then, especially because they were smooth and symmetrical, a *congenital* origin was postulated.^{6,8} For various and valid reasons anatomists cast some doubt on this hypothesis, and returned to a



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FIG. 2. "Wedge-shaped" fifth lumbar body. Horizontal type of sacrum. Note that the fifth lumbar body is not foreshortened (retouched).



FIG. 3. "Hatchet-shaped" fifth lumbar body. This type is commonly foreshortened caudally, and often results in an appearance suggesting slight spondylolisthesis. There is a second type of hatchet shape in which the body is foreshortened at its upper or cephalic end; this is rare and not a source of confusion in the diagnosis of slip.



FIG. 4. Caudally foreshortened fifth lumbar body. This is the type which may result in an erroneous diagnosis of spondylolisthesis when neural arch defects are present.

PATHOLOGIC CLASSIFICATION

The pathology may be considered under four stages: minimal, early, moderate and advanced. Most of the cases we have seen in the last two years in Naval Hospitals are classifiable as *minimal*. Many of these have been discharged from service; some returned to duty, often limited duty.

These minimal cases show a defect in one or both halves of the neural arch (usually both) of a lower lumbar vertebral segment. The posterior one-third of the segment is retained in more or less normal alignment (by the various spinal ligaments attached thereto, the capsular, interspinous, and supraspinous ligaments). The anterior two-thirds of the segment show a forward displacement of 1 or 2 mm., sometimes increasing in the erect position* or with heavy

* Some authors stress that recumbent lateral projections should be made with the legs *extended*, instead of the usual slightly flexed position. After making projections in both poses in a series of cases, we abandoned the extended one because (a) there was no

traumatic explanation—infantile or birth traumata with actual fractures or local osteochondral vascular disturbances of the neural arch.^{1,8,9} Some are undoubtedly due to adolescent or adult injuries of an unusual type. It is conceivable to us, but naturally very difficult of proof, that *strain or deficiency* fractures may explain many cases, especially in the presence of suitable anatomic conditions. The latter would include a congenitally slender isthmus plus a poor blood supply. The critical nature of the blood supply to the neck of the femur is well known. It is quite possible that in some individuals the vascular supply of the interarticular areas of the neural arches of the lower lumbar vertebrae is equally critical. If so, this would explain the failure of fractures in these areas to unite readily, and hence the permanent clefts.

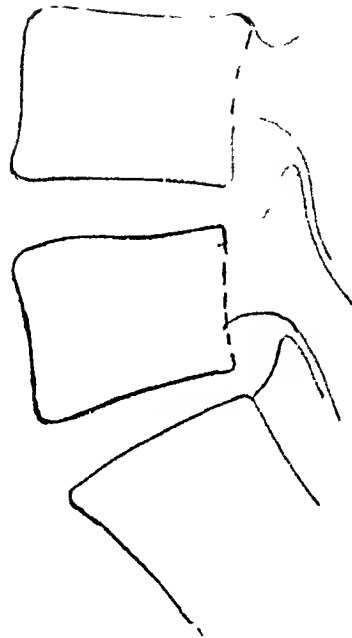


FIG. 5. Generally foreshortened fifth lumbar body. This type also leads to an erroneous diagnosis of spondylolisthesis. Its posterior surface lies on a plane anterior to that of the first sacral, but its anterior surface is not truly displaced. Note that the sacrum is of the vertical type.

weight bearing. There may be slight posterior narrowing of the subjacent intervertebral disc. There are usually no osteophytes on the anterior superior margin of the subjacent vertebral body, nor sclerotic changes in its superior horizontal surface.

When the arch defect is unilateral, the involved body may, if it slips at all, rotate slightly to the unaffected side, rather than forward; this we have seen only once.

In addition to the cleft or clefts in the neural arch, there may be one in the spinous process; one or more of the articular processes may be aplastic, and other anomalies may be present. Incidentally, such associated findings, when present,

significant change in the lumbosacral angle in most cases and (b) motion was difficult to eliminate in extension. Other authors stress that *erect* lateral projections should be made as a routine; such erect views are of value in demonstrating gliding in some cases, but are really *necessary* only in cases with established arch defects and *questionable* slip.

have lent support to the hypothesis of a congenital origin for the interarticular defects, despite anatomists' objections that there is no developmental reason for them.

The arch defects may involve *two* adjacent lumbar segments in a strikingly similar manner—smooth, slender, oblique fissures in the interarticular portions of the fourth and fifth lumbar segments, or other adjacent segments, without associated evidence of trauma.^{4,13,19}

At the other end of the pathological scale are seen the advanced cases, as first described by Killian¹⁰ in 1853*, and beautifully illustrated in the classical monograph of Neugebauer¹⁶ in 1882. The advanced cases show marked forward displacement and sometimes downward tilting of the in-

* The term spondylolisthesis or gliding vertebra was first used by Killian in 1853. The condition itself had previously been mentioned by Herbineau in 1782, Rokitanski in 1839 and Belloc in 1849.³

volved vertebral segment, variable degrees of thinning of the subjacent disc, sclerosis of the superior surface of the slipped body, gross distortion of the neighboring ligaments and other soft tissues (including variable degrees of stretching or compression of the segmental spinal nerves). There is usually much new bone formation on both the first sacral and fifth lumbar bodies. The slipped body may even overlap the mid-sacrum.

In the intermediate stages (early and moderate) the changes are correspondingly less or more marked, depending in part on the amount of associated, coincidental trauma, the physiological status of the patient, and the presence or absence of complicating inflammatory disease.

The fifth lumbar body is sometimes abnormal in shape (shortened, markedly wedged, or hatched shaped). The foreshortening is usually on a congenital basis. The wedge shape is nearly always similar

in origin and often accompanied by a horizontal type of sacrum. The hatchet shape may be congenital or acquired, the latter developing especially in cases of long-standing true slipping.

DIAGNOSIS

The diagnosis of minimal or early cases of spondylolisthesis is largely a roentgenological problem. The essential criteria for the establishment of a diagnosis of true slip are the roentgen demonstration of (a) unequivocal forward displacement of a vertebral body, in the presence of (b) a defect, or defects, in the interarticular portions of the neural arch of that segment.

The first requires a correctly positioned and exposed lateral roentgenogram of the lumbosacral spine, made sometimes in the erect as well as the horizontal position (since some slips are evident only in the erect position). The second requires oblique projections of the lumbosacral area made

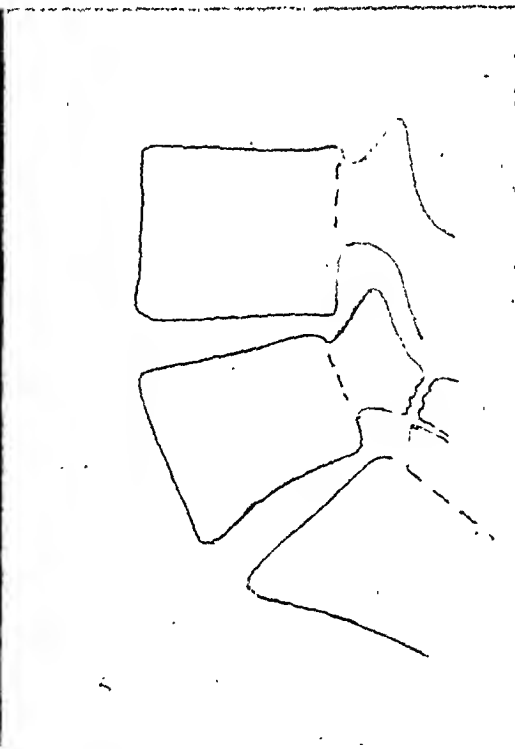


FIG. 6. Neural arch defects in the fifth lumbar, without slip. By former standards, relying on the plane of the posterior surface of the fifth lumbar, a grade 1 spondylolisthesis would be reported in a case of this type. Close inspection reveals that the fifth lumbar body is foreshortened, and that its anterior margin is *not* displaced.



FIG. 7. Neural arch defects in the fifth lumbar, with slip. Spondylolisthesis, partial grade 1, slip about 4 mm.

FIG. 8. Same case as Figure 7, showing use of rectangular test line. In this case, the anterior inferior edge of the fifth lumbar body crosses the test line (instead of lying from 1 to 5 mm. behind it). This is a fairly reliable index of true slip, subject to the anatomical restrictions mentioned in the text.

with the patient at the optimum angle to show his particular defect, an angle found only by trial and error, but usually in the range of 35° to 50° with the horizontal. The defects may be visible in the anteroposterior views, but should always be confirmed by oblique projections, except in advanced cases.

In addition to the above criteria, the following findings are sometimes of value, especially in the more advanced cases, and may be seen in routine anteroposterior views: (c) overlapping of the shadows of the transverse processes of the involved segment on those of the subjacent one, (d) obscuration of the margins of the involved body; this body may be "invisible" in the anteroposterior view or may show as a crescentic shadow overlying the subjacent one (Brailsford's "bow" line), (e) apparently increased density of the fifth lumbar body, owing to the overlapping.

These latter findings will be enhanced in subjects with an acute lumbosacral angle. When the sacrum is of the "vertical" type

its superior surface tends to be horizontal and give good support to the spine in the erect position; when the sacrum is of the "horizontal" or sharply angulated type (in reference to the lumbar spine), its upper surface naturally gives less support to the spine above, and more readily allows a slipping fifth lumbar body to glide forward. Conversely, in patients with a horizontal type of upper sacrum, the more easily will such a slip be detected in routine anteroposterior roentgenograms.

DISCUSSION

Upon what criteria can the detection of slight forward slipping of a fifth lumbar body be based? If the posterior edge of this body is forward in relation to the posterior margins of the first sacral body, but its anterior margin is not displaced, is there a true slip? We believe that there is *not*, for the following reasons: Examination of the roentgenograms of the lumbosacral spine of many hundred individuals with and without backache discloses the fact that a small

but significant percentage of persons have a foreshortened fifth lumbar body, and, apparently, relatively elongated pedicles. When no arch defects are present, this ana-



FIG. 9. Neural arch defects, with slip (spondylolisthesis grade II). Note the overlapping of the shadows of the fifth lumbar transverse processes on those of the first sacral; the obscuration of the outlines of the fifth body; the apparent increased density of the fifth body, and the angulation and crowding of the laminae and spinous processes of the lower lumbar vertebrae—all indirect signs of slip in the anteroposterior projection.

tomic variation is usually overlooked, or at least not mentioned. However, when arch defects are present, the attention of the examining roentgenologist tends to be focused on the associated problem—slipping. He then notes the apparent displacement of the fifth body (as judged by its posterior margin), ignores the absence of displacement of its anterior margin, and reports “spondylolisthesis, grade I.”

Anterior Margin Displacement. What are the criteria for determining forward displacement of the anterior margin of a lumbar body? In the case of segments above the fifth, the problem is usually simple: one can usually employ the anterior margin of the subjacent lumbar body as a base line. However, in the case of the fifth lumbar body, a base line or norm is difficult to establish. After trial of various methods, we decided on the use of a line drawn perpendicular to the upper surface of the first sac-

ral body, at its anterior superior margin. We found that in all normal individuals (that is, persons without spondylolisthesis, etc.) the anterior inferior margin of the fifth lumbar body lay from 1 to 8 mm. behind this line. In persons with fifth lumbar bodies of normal length and any definite degree of spondylolisthesis, the anterior inferior margin of the displaced body always touched or lay in front of this line.

On reviewing the literature, we find that this line was reported over twenty years ago by Ullmann¹⁸ but has apparently not been generally used. Capener,⁵ Brailsford,³ and Mitchell¹⁵ reported somewhat favorably on its use; Glorieux and Roederer,⁸ Bowman and Goin² unfavorably. Its delineation requires *adequately exposed, true lateral* roentgenograms, centered over the lower lumbar spine and preferably at a distance of at least 36 inches. In a minority of cases the line may be difficult or impossible to establish because of one or more of the following reasons:

(1) The anterior superior margin of the first sacral segment may have a blunt, rounded profile.

(2) This margin may have an osteophyte on it. (Actually, this complication is un-



FIG. 10. Lateral projection of same case as Figure 9, showing neural arch defects, molding of the inferior surface of the fifth lumbar, thinning of the disc, sclerosis of the adjacent body margins and rounding of the superior surface of the first sacral. The test line is never required in gross cases of this type.



FIG. 11, *A* and *B*. Spondylolisthesis grade 1, partial, slip about 2 mm. This case is shown to illustrate the fact that many cases of slip with apparent unilateral arch defects can be shown to have bilateral defects if adequate study is made. The defect in the left side of the neural arch is visible in the anteroposterior view (*A*) but not that in the right (*B*).

sual in the minimal or early cases of olithesis, which are the only ones in which the vertical test line assumes any importance. In patients with such degrees of slip that the first sacral segment shows new bone production, the question of definite diagnosis rarely arises.)

(3) The superior surface of the sacrum may be convex, concave or sinuous in profile, and the base line may be difficult to establish. In such cases one uses the anterior and posterior edges of the segment and draws a line between them. The perpendicular test line is then erected on the anterior end of this line.

(4) When the sacrum is of the extremely horizontal type, its superior surface is almost vertical, and the resultant test line may be deceptive. In such cases its use becomes of doubtful validity.

(5) A markedly wedge-shaped last lumbar disc (narrow posteriorly and wide anteriorly) may produce similar complications.

(6) Finally, a fifth lumbar body with unusually flared lower margins may, even in the absence of any arch defects, give a "positive" result in the presence of a vertical type of sacrum.

Despite the above complexities, the vertical test line may be established in the majority of correctly made lateral roentgenograms of the lumbosacral spine, and true ventral displacement of the fifth lumbar body may usually be diagnosed when the anterior inferior margin of the body with neural arch defects lies anterior to it.*

Posterior Margin Displacement. The posterior margin of the fifth lumbar body in most normal individuals bears a linear relationship to that of the first sacral. A smooth, continuous curved line will result from joining their respective upper and lower posterior edges. However, in a small

* Method. In actual practice, we mark with wax pencil the anterior and posterior margins of the upper surface of S_1 and the lower anterior margin of L_5 on the lateral film. Then we use a transparent rectangular guide, with millimeter scale, a cleared 5x7 inch film makes a convenient test "ruler."



FIG. 11, C and D. Left posterior oblique views (about 40°) showing large gap in left neural arch of same case.

but definite percentage of individuals the fifth lumbar body will show variations in shape and size which render quite void the use of these landmarks to determine slip. Most of these individuals have a foreshortened fifth lumbar body. The body may be foreshortened generally or just in its caudal half. As a result, its posterior inferior margin will lie on a plane ventral to that of the first sacral, and the physician glancing casually at the roentgenogram will conclude that a grade 1 spondylo-olisthesis is present. The proof, in such cases, that slip is not actually present is obtained from the fact that the anterior edge of the body is not in front of the perpendicular test line.

Conversely, it is to be recognized that slip might be present (the anterior inferior edge of the fifth lumbar crossing the test line), but the posterior margin of this body appear to be in alignment with that of the first sacral. This could occur in very rare cases of platyspondyly of the last lumbar segment, or could apparently be present

when new bone production results in formation of a spur or ridge on the posterior inferior margin of the body of the fifth lumbar body. We have seen examples of the latter, but not of the former.

The foreshortened fifth lumbar body is often associated with a wedge or hatchet shape in profile view. In long standing cases of olisthesis, it is quite common to see compression of the posterior and inferior surfaces of the fifth body, as a result of repeated gliding traumata. The associated bony changes (sclerosis, osteophyte production, etc.) will nearly always serve to distinguish this acquired hatchet shape from the true congenital type. The important element in the disturbed shape is the foreshortening of the caudal half of the body.

We studied the lumbosacral spine roentgenograms of 170 consecutive cases in an effort to establish data for measurement of this foreshortening, comparing the respective lengths of the last lumbar and the first sacral bodies. The subjects were mostly white males, between the ages of eighteen

and forty years, of average height and weight (that is, there were no grossly overweight individuals, and no skeletal freaks in the group). About 10 per cent of them were females. The following facts were found:

(a) The *length* of the fifth lumbar body: There were 61 cases in which the inferior margin of the fifth lumbar body was from 1 to 10 mm. shorter than that of the superior margin of the first sacral body. Counting only those cases in which the difference in length was 3 or more millimeters, there were 25. That is, approximately 15 per cent of the group showed notable and potentially significant *foreshortening* of the fifth lumbar body.

There were 36 cases in which the two margins were identical in length.

There were 73 cases in which the inferior margin of the fifth lumbar body was from 1 to 4 mm. longer than the first sacral. If we include only the cases with a difference of 3 or more millimeters, there were 23.

That is 13 per cent of the group showed slight elongation of the fifth lumbar. None of this particular group showed any significant degree of platyspondyly.

(b) The *shape* of the fifth lumbar body: There were 146 cases with a normally "rectangular" fifth lumbar body, and 24 cases (14 per cent) with a more or less hatchet-shaped body. Actually, most fifth lumbar bodies that "look" rectangular in lateral projections are found by measurement to be slightly wedge shaped, i.e. the vertical dimensions of their posterior margins are from 2 to 8 mm. less than the vertical dimensions of their anterior margins, *but they are not caudally foreshortened*. It is this foreshortening (either caudal or general) that causes confusion in the diagnosis of slip, and that produces the appearance we term "hatchet shaped."

In an attempt to establish figures that might be of value in determining foreshortening, the sagittal lengths of the inferior margins of the fourth and fifth lum-

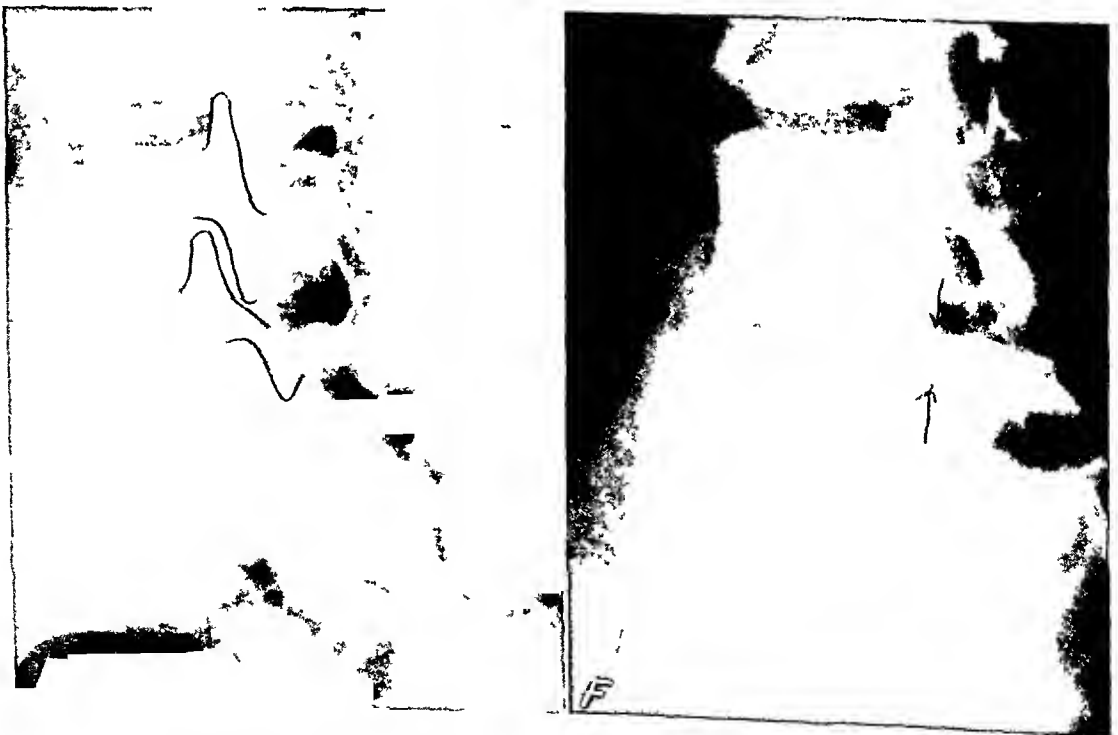


FIG. 11, E and F. Right posterior oblique views (E at about 40°, F at 60°). The fine cleft in the right side of the neural arch is only visible in the latter projection. Same case as preceding.

bar bodies and of the superior margins of the first sacral body were recorded in millimeters directly on lateral roentgenograms, made at 36 inch distance. In 3 cases, multiple lateral exposures were made, centering

It is evident that when the fifth lumbar body has a conventional shape, it tends to be of the same length as the first sacral, but that when it has a hatchet shape, it tends to be on average 2.2 mm. shorter. It is noteworthy that this foreshortening is also evident on comparing the length of the fifth body with that of the fourth. Therefore, the presence of a hatchet-shaped body gives a visible clue to the presence of potentially significant foreshortening.

(c) The relative *position* of the fifth lumbar body: The question of true slip and pseudo slip was next analyzed. In the entire group of 170 cases, there were 20 with bilateral defects in the neural arch of the fifth lumbar (12 in the group with normal-shaped bodies, 8 in the group with hatchet-shaped bodies). Of these 20 with defects, only 8 showed spondylolisthesis according to our criteria (i.e. forward displacement of the fifth lumbar body as judged by the location of its *anterior* as well as its posterior margins). But, had we been guided by generally accepted procedures, and used the posterior margin of the fifth lumbar as the main criterion, 13 of them would have been classified as grade 1 olisthesis.

The relation of the perpendicular test line to the anterior inferior edge of the fifth lumbar body was as follows (all measurements in millimeters directly on 36 inch distance lateral roentgenograms (Table II).

The relationship of the posterior edge of the fifth lumbar to that of the first sacral body was also recorded directly on the roentgenograms in millimeters. The results shown in Table III were obtained.



FIG. 11, G. The fine cleft in the right side of the neural arch is slightly retouched. Same case as preceding.

at the mid-lumbar, the lower lumbar and finally the upper sacral planes. These variations in centering did not produce significant alterations in the recorded measurements. The figures obtained are given in Table I.

TABLE I

Group	Length of Margins of	Average	Maximum	Minimum
Normal-shaped bodies (L5)	L4 inferior	45.6	58	36
	L5 inferior	44.2	55	35
	S1 superior	44.5	52	37
Hatchet-shaped bodies (L5)	L4 inferior	44.4	50	39
	L5 inferior	42.2	50	37
	S1 superior	44.4	52	37

In the foregoing discussion and, indeed, throughout most of this paper, the expression fifth lumbar vertebra is used to denote the last free lumbar segment. Other things being equal, similar remarks would apply to either the fourth or sixth lumbar segment, in cases with that number of segments, and in whom the problem of determining slip arose. It is for purposes of simplicity that the term "fifth lumbar" has been adhered to throughout.

TABLE II

Group	Perpendicular Test Line in Front of Anterior Inferior Margin of Fifth Lumbar		
	Average	Max.	Min.
In 150 cases without arch defects	3.6 mm.	8	1
In 12 cases with arch defects but no true slips	2.0 mm.	5	0
In 8 cases with arch defects, and true olisthesis	-3.0 mm.	-9	0

In cases with spondylolisthesis of a vertebral segment proximal to the last free lumbar segment (usually the third or fourth lumbar body, in patients with the normal number of lumbar segments), the problem of detecting slip is much easier, except when the subjacent disc is extremely wedge shaped and the superior horizontal surface of the subjacent body tilted downwards anteriorly to a marked extent. In the latter event a perpendicular test line may be of use. The apparent length and shape of the involved body should always be noted (since the third or fourth lumbar body may itself be hatchet shaped and foreshortened).

It is interesting and noteworthy that a foreshortened lumbar body, in the absence of olisthesis, is usually correctly aligned anteriorly; its posterior margin is almost invariably the one which is out of line, being ventral to those of its fellows.

TABLE III

Group	Relation of Posterior Surface of Fifth Lumbar to Posterior Edge of First Sacral
In 150 cases without arch defects	110 showed normal alignment 10 were anterior to S ₁ (1-3 mm.). That is, these cases had foreshortened bodies and would have been erroneously labeled slips if defects had been present (pseudospondylolisthesis) 30 were posterior to S ₁ (2-7 mm.). That is, these cases had slightly <i>elongated bodies</i> or anomalous facets were present. Some would call them "reverse spondylolisthesis" had arch defects existed
In 12 cases with defects, but no true slip	5 were anterior to S ₁ (2-3 mm.). The bodies were foreshortened; there was no visible displacement anteriorly (no true slip)
In 8 cases with spondylolisthesis (7 grade I, 1 grade II)	8 were anterior to S ₁ (2-9 mm.)

Meschan* has recently reported an improved method of posterior margin mensuration using two lines: the first line is drawn from the posterior inferior margin of the body above the suspected segment of the posterior superior margin of the body below that segment; the second line joins the posterior superior and posterior inferior margins of the suspected segment. These two lines may form an angle or lie parallel with each other. Meschan believes that slip is present (*a*) when an angle is formed with the apex falling above the involved body (and not present when it falls below that body), and (*b*) when the lines are parallel but separated 4 or more millimeters. He classifies an angle of less than 10° as slight slip, 11°-20° as moderate and over 20° as severe. If erect lateral roentgenograms (made in neutral or hyperextended posture) reveal an increased angle he regards the lumbosacral angle as "unstable."

The reliability of these lines were checked by the author with the following results:

(1) In 7 cases of definite slip (mostly partial grade 1) the angle was positive in all; however, the classification as to degree of slip did not agree with conventional ones; in 3 cases of only *slight* slip (of about

* Meschan, I. Spondylolisthesis. *AM. J. ROENTGENOL. & RAD. THERAPY*, 1945, 53, 230-243.

2, 3 and 9 mm. respectively) the angle measured moderate slip (15° , 11° and 12°).
(2) In 6 cases of unilateral or bilateral arch defects without slip, the angle was positive in 1 and parallel lines were 5 mm. apart in 2; of these cases, 2 had foreshortened fifth lumbar bodies.

of 18 cases a negative "Meschan" test was found to be reliable in excluding slip in 7, but a positive test appeared to be somewhat unreliable in 11. Of these 11 "positives" only 7 had demonstrable slip by our standards; the test was therefore unreliable in about one-third of this small group of cases.

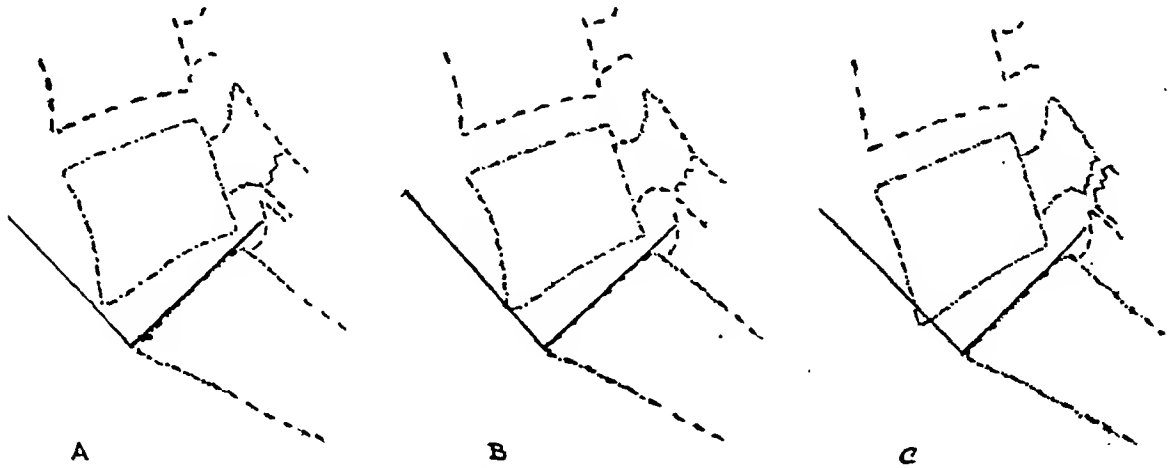


FIG. 12. Diagram to illustrate the use of the right-angle test line.

- A, neural arch defects without slip. Note that the anterior margin of the fifth lumbar body lies about 3 mm. behind the test line.
- B, neural arch defects without definite slip. The body of the fifth lumbar does touch the test line but its posterior edge is not significantly out of line and none of the other findings of olisthesis (see text) are present. Occasionally, cases of this type can be shown to slip slightly in the erect position.
- C, spondylolisthesis, partial grade 1. The anterior margin of the body of the fifth lumbar crosses the test line.

(3) In 5 cases without defects, the angle was negative in 4 and positive in 1 (10° !); the latter was a case with an unusually greatly foreshortened fifth lumbar body.
In summary in a small but carefully studied series

General Data on Spondylolisthesis. The following additional statistical data bear on the general problem of spondylolisthesis and are noted here for the reader's information:

TABLE IV
VERTEBRAL SEGMENT INVOLVED IN SPONDYLOLISTHESIS*

Reference	Number of Cases	Percentage Incidence of Involvement Per Lumbar Segment						
		5†	4	3	2	1	5 and 4	3 and 2
Willis ¹⁹	79	91	5	1	0	1	1	0
Burckhardt†	63	73	17	3	0	0	5	2
Garland ⁷	38	74	18	0	2	0	3	0
Garland and Thomas (present paper)	8	87	13	0	0	0	0	0
Meyerding ¹⁴	583	82	11	0.5	0.3	0	4.4	(double)**

* It is probable that some cases of "pre-" or pseudo-spondylolisthesis are included in Willis', Burckhardt's and Meyerding's figures. Our figures, in this table, list only cases of true slip as defined in this article.
† Or of last free lumbar segment.
** Exact location not specified.

Incidence of neural arch defects: Approximately 6 per cent of human skeletons (Willis¹⁹). Stewart¹⁷ found them in 20 per cent of Eskimo skeletons. They are seen more commonly in persons with an increased number of presacral segments. We found them in 11.7 per cent of our series of 170 cases referred for lumbosacral spine examinations. Several were difficult to demonstrate and might have been overlooked if we had not been interested in the problem involved.

Anatomical location of the olisthetic segment: About 80 per cent involve the fifth lumbar vertebra; most of the remaining 20 per cent involve the fourth. Isolated cases have been reported involving the third, second and first lumbar bodies, respectively (Burckhardt, Willis, and others).^{4,14,19} There are occasional cases of double displacement of two adjacent lumbar segments. Independent of the present series, we have seen one double slip of the fourth and fifth lumbar, and one isolated slip of the second lumbar.

Arch defects: In about 95 per cent of true olistheses the neural arch defects are *bilateral*; In the remainder the defects are or appear to be *unilateral*. The figures in the literature⁶ are 75 per cent bilateral defects, 25 per cent unilateral; this has *not* been our experience. By making additional oblique projections at different angles we believe that most apparently unilateral cases will be found to be bilateral, at least, in cases of true slip.

Age factor: Until recent years some 50 per cent of cases were first noted in the third and fourth decades. Data from various military hospitals (including our own) suggest that this figure will soon be revised to read about 80 per cent of cases in those decades. The majority of the remainder occur in the ensuing decades. Kleinberg¹¹ reported in 1933 that there were no cases on record under the age of ten, but the next year he reported 1 case in an infant of seventeen months (grade II, discovered incidentally).¹² In 1940 Hitchcock⁹ saw a case

of neural arch defects without slip in a patient aged four.

Sex factor: Spondylolisthesis was once considered a predominantly female disorder. Recent literature gives a ratio of 76 per cent in males to 24 per cent in females. It is probable that the true ratio is closer to 50-50 (see also Hitchcock).⁹

Degree of slip:: According to the literature, some 30 per cent of cases show a grade I displacement (Meyerding).¹³ Using our criteria we believe that the figure is closer to 80 per cent. Age and occupation will doubtless influence this element considerably. The older the patient, the greater the occupational or physiological strain (heavy work, multiple pregnancies), the higher the incidence of grade II and III slips. Grade IV slips are relatively rare, although several are on record.

SYMPTOMS

This highly controversial aspect of the subject will not be dealt with in the present paper, which is concerned essentially with the more accurate diagnosis of early cases. Suffice it to say that experienced roentgenologists and other physicians have reported extreme degrees of spondylolisthesis (grade IV) in persons without any symptoms referable to the spine or legs, while, on the other hand, some orthopedists have attributed "severe disabling symptoms to very slight degrees of slip" (grade I).^{*} It is our personal *impression*, based on private practice, previous general hospital and current naval hospital experience, that the vast majority of grade I lesions are *not* symptomatic.

SUMMARY

The roentgen diagnosis of spondylolisthesis should only be made when the vertebral body under suspicion can be shown to be actually displaced anteriorly in relation to the subjacent one.

The essence of olisthesis or slipping is

^{*} Quoted by Bell, J. C., and Heublein, G. W., *Radiology*, 1944, 43, 444.

that the whole vertebral body, and not just its posterior surface, is displaced anteriorly.

The confirmation of such displacement is aided, in early and minimal cases, by measuring the distance from the anterior inferior margin of the suspect segment to a line drawn perpendicular to the anterior margin of the subjacent uninvolved one (called the perpendicular test line). If the apparently displaced body does not touch or lie anterior to this line, it is not truly displaced, in the vast majority of instances. If the displaced body does cross it, a slip is virtually always present.

The reason why spondylolisthesis grade 1 is frequently reported, when it is not actually present, is that the body of the fifth lumbar (or involved segment) is *foreshortened*, so that while its posterior edge lies ventral to that of the subjacent segment, its anterior edge actually does not.

In view of the serious psychic and economic hazards sometimes ensuing from the use of the term spondylolisthesis, and implied (to inexperienced minds) by the term prespondylolisthesis, we believe neither diagnosis should be made casually.

If a true slip is present, it should be reported and the approximate degree of slip recorded in mm. (the term grade 1, popularly applied to slips involving up to one-fourth the sagittal diameter of the upper surface of the first sacral body, covers such a wide range that its usefulness is limited; if used, it should be qualified by words such as "partial" or "complete," and the approximate number of millimeters of slip noted).

If neural arch defects exist but no true slip is present, it would be correct to record the defects (e.g. "bilateral fissures in the neural arch of the fifth lumbar without visible displacement of the body") and omit the term prespondylolisthesis, especially since the case may never actually progress to slipping.

In a review of 170 consecutive lumbosacral spine roentgen examinations (made in reference to claimed backache or injury), it was found that 25 persons or 14.7 per

cent had more or less *foreshortened* last lumbar segments. In 15 of these no neural arch defects were present, but the posterior edge of the last lumbar body lay from 1 to 3 mm. ventral to the plane of that of the first sacral. In the other 9, arch defects were present, but in only 4 was the *anterior margin* of the fifth lumbar body ventral to the test line (that is, only 4 of the 9 showed true spondylolisthesis). There were an additional 4 cases of true slip with bodies of "normal" shape and length.

The remainder of the 170 cases, or 85.3 per cent, had last lumbar bodies that were either normal in shape and length or, in some instances, a little elongated, so that their posterior margins lay on a plane slightly behind that of the first sacral.

It may be stated that, in general, if the fifth lumbar body is normally "rectangular" in shape, and proportionate in size to its adjacent segments, there is a slip (olisthesis) *only* when its anterior margin reaches or passes the *perpendicular test line* drawn from the first sacral.

If the fifth lumbar body is foreshortened (especially caudally), and its shape in lateral projection is hatchet like, the relation of its posterior margin to that of the first sacral *cannot* be relied upon for the detection of slip. In extreme cases of foreshortening, its anterior margin might be equally unreliable, but such cases are very rare, since, as we have shown, the anterior margin of a foreshortened body is almost always correctly aligned anteriorly. Hence, strictly speaking, neither the anterior nor the posterior margin measurements are criteria in *all* cases, but, in the vast majority, the anterior margin measurements are the more reliable.

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LUMBOSACRAL ROENTGENOGRAMS OF ONE HUNDRED SOLDIERS

A CONTROL STUDY*

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INTRODUCTION

BACKACHE has been the subject of numerous roentgenographic studies. Injuries, faulty posture, congenital anomalies and disease have been described as causes of low back pain but there are many instances of backache in which no anatomic abnormality can be found. Conversely, roengenograms of the lumbosacral region made for reasons other than for backache have disclosed defects and variations which do not cause symptoms.^{5, 9, 13, 19} As the part of an investigation into the causes of backache among military personnel, 100 soldiers were examined as controls. The purpose of this paper is to present the abnormalities found in the roentgenograms of the lumbosacral region of this group.

MATERIAL

The subjects examined were all males between the ages of nineteen and thirty-

lumbar spine and sacrum in anteroposterior and lateral projections; (2) a roentgenogram made with the roentgen tube tilted cephalad at a 30 degree angle to show the sacrum, sacroiliac joints and the relationship of the transverse processes of the last lumbar segment to the lateral masses of the sacrum; (3) roentgenograms made in right and left semilateral projections with the subject rotated 30 to 45 degrees, for visualization of the laminae of the vertebral arches and the articular processes with their facets (Fig. 1). All of the roentgenograms were studied by each of us. In cases where there was any doubt as to the nature of an abnormality, stereoscopic roentgenograms and roentgenograms made in other projections were obtained for further study. Table II contains the details of the anatomical variations found in the roentgenograms of the entire group. Table III summarizes the principal abnormalities.

TABLE I

Age	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39
Number	6	6	5	8	8	4	9	7	7	9	3	7	2	7	1	2	1	2	4	1	1

nine years with an average age of 26.6 years. The age distribution is seen in Table I. With few exceptions these men had been subjected to strenuous military training and some had been in combat. Each was carefully interrogated with reference to back pain, recent or old, and any history of trauma to any part of the back. Only those who never had backache or suffered an injury to the back were included in this study. The roentgenograms which were obtained in each of the subjects consisted of: (1) routine views of the lower

SPONDYLOLYSIS AND SPONDYLOLISTHESIS

Defects of the neural arch of the lower lumbar spine are not uncommon. The defect in the arch to which the term spondylolysis has been applied consists of an interruption of the bone between the inferior and superior articular processes, the pars interarticularis. This results in a division of the vertebra into two separate parts, the anterior portion consisting of the body with the pedicles, transverse processes and superior articular processes and the posterior portion which consists of the

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TABLE II

Variations	No. of Spines
No variations	20
Generalized osteoporosis, slight	1
Congenital absence of inferior articular facets of L ₅ . Spondylolisthesis of L ₅ upon S ₁ , Grade II; L ₅ is wedge shaped and sacralized; failure of fusion of the arch of L ₅ in region of laminae; lumbosacral joint narrowed posteriorly; spina bifida of sacralized L ₅ ; acuity of lumbosacral angle increased	1
Spondylolysis of the arch of L ₅ , bilateral; spondylolisthesis, Grade II; marked narrowing of lumbosacral joint; spina bifida of all sacral segments; degenerative changes and lipping about adjacent articular margins of L ₅ and S ₁	1
Spondylolysis of arch of L ₅ , bilateral; spondylolisthesis of L ₅ upon S ₁ , Grade I; asymmetrical facets; increased obliquity of superior surface of sacrum	1
Spondylolysis of arch of L ₅ , bilateral; first degree forward, spondylolisthesis of L ₅ upon S ₁	2
Spondylolysis of L ₅ , unilateral; Schmorl's nodule on inferior surface of L ₅ ; asymmetrical facets, lumbosacral articulation; spina bifida of S ₁	1
Schmorl's nodules on inferior surfaces of L ₃ , L ₄ and L ₅ ; asymmetrical facets	1
Schmorl's nodule inferior surface of L ₅	2
Schmorl's nodule inferior articular surface of L ₃ , L ₄ and L ₅	1
Unilateral (left) sacroiliac arthritis; asymmetrical facets, lumbosacral articulation	1
Degenerative arthritic changes about adjacent articular margins of L ₅ and S ₁	1
Transitional vertebra; spina bifida occulta of S ₁	1
Unilateral sacralization of L ₅ formation of false joint with degenerative changes	1
Increased acuity of lumbosacral angle	1
Schmorl's nodule on inferior surface of L ₃ ; spina bifida occulta of S ₁	1
Schmorl's nodule on inferior surface of L ₅ ; spina bifida occulta of S ₁	1
Narrowing of lumbosacral joint	1
Marked narrowing of lumbosacral joint and between bodies of L ₄ and L ₅ ; degenerative arthritic changes are present about articular margins of L ₄ , L ₅ and S ₁	4
Moderate narrowing of lumbosacral joint and degenerative arthritic changes between adjacent articular margins of L ₅ and S ₁	1
Unilateral sacralization of fifth lumbar slight narrowing of lumbosacral joint; asymmetrical facets, lumbosacral articulation	1

TABLE II—Continued

Variations	No. of Spines
Transitional vertebra; asymmetrical facets; lumbosacral articulation; spina bifida occulta of S ₁	2
Ununited left inferior articular process of L ₄ ; asymmetrical facets; spina bifida occulta of S ₁ , lumbosacral articulation	1
Spina bifida occulta of first sacral segment	12
Spina bifida of S ₂ , S ₃ , S ₄ and S ₅	1
Spina bifida occulta of L ₅	1
Spina bifida occulta of S ₁ ; slight narrowing of lumbosacral joint	2
Spina bifida occulta of S ₁ ; asymmetrical facets, lumbosacral articulation	7
Spina bifida occulta of S ₁ ; asymmetrical facets; lumbosacral articulation; Schmorl's nodule on inferior surface of L ₅	2
Failure of fusion of left inferior articular process of L ₂ ; spina bifida occulta of S ₁	1
Unilateral sacralization of L ₅	2
Transitional vertebrae	2
Transitional vertebra; asymmetrical facets, lumbosacral articulation	1
Asymmetrical facets between L ₅ and S ₁	21

TABLE III

Variations	No. of Spines
Spina bifida occulta	36
Narrowing of lumbosacral joint	11
Asymmetrical facets	39
Degenerative arthritis of lumbosacral joint	4
Sacroiliac arthritis	1
United epiphyseal centers	2
Transitional vertebrae	11
Increased acuity of lumbosacral angle	2
Spondylolysis	1
Spondylolisthesis	1
Schmorl's nodules	5
Generalized osteoporosis	8
	1

laminae, spinous process and inferior articular processes. The etiology of this defect in the neural arch is still under dispute.^{3,20,37} Spondylolisthesis is a better known term. It generally consists of a forward displacement of the fifth lumbar vertebra and spine upon the sacrum because of a congenital abnormality or injury. Less frequently the fourth lumbar segment is displaced and very occasionally



FIG. 1. Roentgenogram of the lumbosacral region made with subject rotated 45 degrees to show the vertebral arch and the articular processes with their facets. There is a wide defect in the arch in the region of the pars interarticularis.

spondylolisthesis is found at other levels. The underlying lesion preceding and resulting in spondylolisthesis is an interruption in the continuity of the neural arch in the region of the pars interarticularis (spondylolysis) or faulty development of the inferior articular processes permitting a forward displacement of the affected segment. Strong ligamentous structures maintain the relationship of the inferior articular processes of the last lumbar vertebra with the articular processes of the sacrum preventing the spine from slipping over the superior articular surface of the sacrum. A spondylolysis disrupts this bony anchorage.

Defects in the pars interarticularis were found in 6 per cent of the spines of the control group. In 1 of the spines the defect in the arch of the fifth lumbar segment was unilateral. This spine also had asymmetrical facets and there was a spina bifida occulta of the first sacral segment. Uni-

lateral defects are not rare. Willis found this abnormality in 25 per cent of spines with spondylolysis. Four of the 6 spines with spondylolysis showed characteristic bilateral defects in the region of the pars articularis of the last lumbar vertebra and some degree of forward displacement upon the sacrum; 3 were of Grade I and 1 was of Grade II severity (Meyerding's classification).

One spine in which a Grade II spondylolisthesis was found presented the degenerative changes frequently seen in this condition (Fig. 2). The anterior margin of the first sacral segment was rounded off and there was a flaring collar-like ridge of excrescent bone formed around the articular margins of the first sacral segment and the overhanging portion of the adjacent articular margin of the fifth lumbar vertebra. These hypertrophic changes were



FIG. 2. Lateral view of the lumbosacral region showing a Grade II spondylolisthesis of the fifth lumbar segment upon the sacrum. The degenerative arthritic changes frequently seen in this condition are present.

limited to the articulation of the fifth lumbar with the sacrum and can be ascribed to local irritation of a chronic type resulting from mechanical strain. The absence of back pain even in the presence of advanced degenerative arthritis and severe grades of spondylolisthesis have been observed by others.^{17,28}

Another spine which showed a Grade II spondylolisthesis had bilateral defects in the laminae. There was also a congenital absence of the inferior articular processes of the fifth lumbar vertebra mentioned by Goldthwait¹⁴ and Müller.²⁸ The mechanism of forward slipping of the fifth lumbar segment in this spine differs from the others in this series and was attributed to the loss of the bony anchorage formed by the inferior articular processes. Normally these are in apposition with the superior articular processes of the sacrum and prevent the lumbar spine from gliding downward and forward on the oblique sacral articular surface.

Roentgenograms of the spines of large groups of men applying for industrial positions have been previously studied by Cushway and Maier,⁹ and Breck, Hillsman and Basom.⁵ All of these men were presumably asymptomatic. The incidence of abnormalities found in these groups varied considerably. In the series of 931 spines examined by Cushway and Maier only 3 instances (0.3 per cent) of spondylolisthesis were found. Breck and his associates found evidence of spondylolisthesis in 3 per cent of the 450 spines which they studied. Other groups studied roentgenographically showed a different incidence of this abnormality. George¹³ found it in 3.5 per cent of 3,301 patients examined for symptoms referable to the lumbar spine. Another series of 500 spines reported by Kleinberg²³ showed an incidence of 2 per cent of spondylolisthesis and 2 per cent spondylolysis. Pheasant and Swenson²⁹ who examined the lumbosacral region of 171 cadavers roentgenographically, 42 of which were prepared, found evidence of spondylolysis in 1.1 per cent. Where large num-



FIG. 3. Anteroposterior view of the lumbosacral region showing a transitional vertebra. The left transverse process impinges on the sacrum forming a false joint.

bers of skeletons were examined the incidence of pars interarticularis defects coincided closely with the number found in the control series. Willis³⁵ found it in 5.19 per cent of 1,520 skeletons and Congdon⁸ who studied the skeletons of 200 American aborigines in the Columbia river region encountered it in 5.0 per cent. Higher incidences of this abnormality are reported by Shore,³¹ who found neural arch defects in 9.1 per cent of 56 Bantu South African native skeletons, and Stewart,³² who reported an incidence of this variation in 39 per cent of 187 spines of Eskimos living north of the Yukon and 14.5 per cent in another series of spines of Eskimos on and south of the Yukon.

Sex has little, if any, influence on the incidence of neural arch defects in the region of the pars interarticularis. Some authors report a greater incidence of this abnormality in males while others find it more frequently in females.^{4,28,38} Chandler⁶ found that it occurred with the same frequency in both sexes.

ASYMMETRICAL FACETS

Asymmetrical facets at the lumbosacral articulations varying from slight to marked were found in 39 per cent of the spines in the control group. Slight variations were found in 27 spines; moderate asymmetry in 8 spines and in only 3 spines were the facets markedly asymmetrical. In addition to the variations observed in the obliquity of the articular facets, variations in their size and shape were found in individuals and in the vertebrae of the same individual. The stability of the lumbar spine, particularly the lumbosacral joint, is affected by the obliquity and direction of the articular facets. For example, facets which are situated in a transverse plane would prevent forward slipping and would allow sidewise displacement. Facets situated in a sagittal plane, on the other hand, would permit forward displacement. In practice, these facets are described as situated in oblique, sagittal or coronal planes but this is inaccurate. Examination of these articulations show that they are frequently curved, each facet corresponding to a segment of a cylinder. Horwitz and Smith²² studied these articulations in cadavers and found that in some instances the superior facets of the lumbar vertebrae were sufficiently curved so that it was impossible for the roentgen rays to pass through the joint space. The shape of the facet as well as its obliquity recorded on the roentgenogram will therefore depend upon which component of the cylinder predominates. Other factors such as the inclination of the sacrum and the angle of projection of the roentgen rays must also be taken into consideration in the interpretation of variations of the articular processes and narrowing or obliteration of the interarticular joint spaces. No evidence of degenerative changes such as osteoarthritis, alteration in the joint space and articular surfaces of the facets and increased density of the adjacent articular surfaces were found in any of the spines studied in this series.

NARROWING OF THE LUMBOSACRAL JOINT SPACE

Some degree of narrowing of the lumbo-

sacral vertebral joint space was found in 11 out of the 100 spines examined. This narrowing was marked in only 2 instances and with them there were degenerative arthritic changes of the adjacent articular margins of the vertebrae. Where there is an unusual amount of stress and strain, such as manifested in these cases, the narrowed lumbosacral joint space can be attributed to degenerative changes in the disc structures and cartilage. Herniation of the nucleus pulposus has been accepted as an important cause of narrowing of the disc space between the last lumbar and first sacral segment but would not explain the changes in many spines.^{7,12} Disintegration of the annulus fibrosus incident to the wear and tear of life is another explanation of a narrowed disc space. Eight of the 11 spines showed only a slight narrowing posteriorly, estimated as about 2 mm. One of these was associated with a transitional vertebra, 4 with spina bifida occulta of the first sacral segment. Narrowed disc spaces are not infrequently found with a transitional vertebra and sometimes present themselves as thin sacral discs.²¹

Congenital narrowing of the joint space, according to Barr and Mixer,² is of rather frequent occurrence, but Vinke and White³³ were able to find only 3 instances in a group of roentgenograms of 300 children between the ages of five and fifteen in whom they were able to exclude other pathological conditions which would cause narrowing of the disc space. Williams³⁴ was able to find only 1 case of congenital narrowing in a like number of roentgenograms.

Prolapse of the nucleus pulposus into the adjacent vertebral body (Schmorl's node) was found in 8 spines. In 6 spines only one segment was affected. In the remaining 2 spines, three vertebrae showed the nodules. Ninety per cent of Schmorl's nodules occur in the lower lumbar spine.²⁵ No secondary changes in the bodies or facets were found with Schmorl's nodules in the control group.

ACUITY OF THE LUMBOSACRAL ANGLE

The acuity of the lumbosacral angle was found to be increased in 2 instances. In

1 of these spines there was a spondylolisthesis. Normally, the lumbosacral angle has an inclination of about 43 degrees but this is not constant. The weight-bearing axis of the spine normally passes anterior to the lumbosacral junction. Therefore, with an increase in the obliquity of the superior surface of the first sacral segment the shearing strain upon the lumbosacral joint becomes greater. This will in turn increase the strain against the posterior articulations which are subjected to added wear and tear. An increased incidence of osteoarthritis would be anticipated with acute sacral inclinations but this does not invariably follow.

OSTEOARTHRITIS

Osteoarthritis of the spine is usually the reaction to changes in the joint cartilages which have undergone degenerative changes attributable to age, trauma or other factors. Marginal bony proliferation of adjacent vertebral borders and osteophyte formation characteristic of osteoarthritis were found in 4 spines. One of these was associated with a Grade II spondylolisthesis; 2 were associated with definite narrowing of the joint space. Osteoarthritis is seen with increased frequency with advancing years. Beginning at about the thirty-fifth year of age, evidence of progressive degenerative changes can be found in the intervertebral joints.³⁶

PERSISTENT OSSIFICATION CENTERS

Persistent ossification centers of the inferior articular process were found in 2 instances, once in the second and once in the fourth lumbar vertebrae. As a rule, these are bilateral and the adjacent surfaces of the ununited ossicle and articular process are smooth and sharply demarcated as compared with the ragged irregular margins of a fracture.³⁷

TRANSITIONAL VERTEBRAE

Transitional type vertebrae were found in 11 spines. Four of these showed unilateral sacralization with long transverse processes. In 1 of the spines (Fig. 2) the transverse process was found to be imping-

ing upon the upper surface of the sacrum producing a false joint. The adjacent surfaces of the impinging bones also showed degenerative changes and evidence of eburnation. Some writers believe that a transverse process which is impinging on the sacrum or ilia can cause clinical symptoms,²⁶ but in general the rôle of a long impinging transverse process as the cause of backache is open to question.^{13,29,30} Spina bifida occulta of the first sacral segment was present in 7 of the 11 spines with transitional vertebrae.

SPINA BIFIDA OCCULTA

The incidence of spina bifida occulta has been reported by Dittrich¹¹ as 5 per cent of all spines examined roentgenographically. Cushway and Maier⁹ found it in 17 per cent of 931 spines; Giles¹⁶ found this anomaly in 23.9 per cent of 1,112 cases; and Breck and his associates⁵ found it in 6 per cent of 450 spines. Meyerding²¹ reported an incidence of 35 per cent of spina bifida occulta of the first sacral segment. The control group showed an incidence of 36 per cent. In 12 of the spines with this variation there were also asymmetrical facets. Other anatomical abnormalities were found in 14 per cent. Two of the spines with spondylolysis and spondylolisthesis in the control group showed this defect in the sacrum and in 1, all the sacral segments were thus affected. One of the spines showing a congenital absence of the inferior articular processes, with other anomalies, also had a spina bifida occulta of a sacralized fifth lumbar segment.

SUMMARY

The abnormalities in the lumbosacral region of the spines of one hundred asymptomatic soldiers have been studied and tabulated.

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OSTEOMYELITIS IN INFANTS

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OSTEOMYELITIS in infants shows anatomical and clinical differences from the disease in older children and adolescents. Prognosis as well as treatment is affected by these differences. These have been recognized by several observers in recent years who have placed the disease in a special category.

ETIOLOGY

The infection is blood borne as in most cases of osteomyelitis at other ages and its origin is thought to be the common respiratory diseases of infants, umbilical and skin infections. Frequently, however, no site of primary infection is found. The causative organism is the hemolytic streptococcus in the majority of cases while *Staphylococcus aureus* is the next most common cause. Green and Shannon⁸ reported 76 cases of osteomyelitis in children under two years of age in which 48 (63 per cent) were due to the streptococcus; 22 (30 per cent) to the staphylococcus; 3 to the pneumococcus and 1 to the gonococcus. Paschlau¹¹ observed 31 cases under one year of age of which 14 were due to the staphylococcus, 5 to the streptococcus, 5 to a combination of streptococcus and staphylococcus and 7 to the pneumococcus. Others, Dillehunt,⁵ Cass¹ and Stone,¹⁴ though with fewer cases, reported a higher incidence of staphylococcus infection, viz., 7 were caused by the staphylococcus and 2 by the streptococcus. Dunham⁶ noted a high incidence of streptococcus in septicemia of the newborn with a distribution as follows: streptococcus 15, staphylococcus 11, *B. coli* 10, pneumococcus 2 and pyocyaneus one.

The dominant rôle of the streptococcus in infants has been explained on the basis of a higher incidence of antecedent upper respiratory infection and relatively less natural immunity to the streptococcus in comparison with the staphylococcus.

PATHOLOGY

Certain anatomic factors contribute to the different nature of the disease in infants. The bone is of a more spongy texture, even in the so-called compact portion, the vascular spaces are larger and the cortex is thinner than in older children. These factors allow a freer communication between the marrow and the subperiosteal spaces.

The mode of infection in osteomyelitis through the capillaries in the juxta-epiphyseal region of the metaphysis is well known. As shown by Starr,¹³ in adolescent osteomyelitis the infection passes more easily through the thin cortex into the subperiosteal space than into the shaft, with early and extensive periosteal elevation. Since the cortex in infants is thinner this is even more apt to occur and the medullary cavity of the diaphysis rarely becomes involved. The periosteum may rupture early with the formation of soft tissue abscesses. There is a minimum of bone destruction and sequestration occurs only in rare instances.

Daubenspeck³ states that osteomyelitis in infants may occasionally arise primarily in the epiphysis and he bases his belief on the experimental work of Shioda.¹² India ink and bacteria were injected intravenously into young rabbits and these substances were found to reach the subchondral spaces of the epiphysis through "sinusoids" of the epiphyseal cartilage, independent of the perforating capillaries. These experiments could not be reproduced in older rabbits. The findings led Daubenspeck to believe that they could be correlated with those found clinically in infants and older children.

Pyarthrosis is a common complication. The infection may reach the joint in one of two ways: (1) It may spread from the

metaphysis through the adjoining epiphyseal cartilage. Since the cartilage is moderately resistant to infection, epiphysiolysis between the metaphysis and the epiphyseal cartilage may occur. More commonly, however, the infection is virulent enough to break through the cartilage into the epiphysis and through it into the joint. (2) In the joints in which the epiphyseal cartilage and a portion of the metaphysis lie within the joint capsule (proximal and distal humeri, proximal and distal femoral joints),⁷ the infection need not traverse the epiphyseal cartilage to reach the joint, but only to break through the periosteum of the metaphysis. The cartilage of the joint is said to be relatively resistant to low grade infection; in virulent infection, however, cartilage as well as the epiphysis is destroyed with resultant deformities and arrest of growth. Serous, aseptic transudates are seen occasionally. These are secondary to the infection near the joint.

Metastatic involvement of other bones—usually of the long bones—is common. Metastatic soft tissue abscesses also occur. Such metastases develop primarily during the stage of septicemia.

Healing occurs rapidly in infants after surgical or spontaneous decompression. The small amount of necrotic bone is usually absorbed and persistent sequestra are uncommon. Formation of new bone is remarkably rapid. Green and Shannon⁸ demonstrated formation of subperiosteal new bone as early as one week following the onset of infection.

CLINICAL COURSE AND TREATMENT

The usual clinical picture in the infant is quite different from that in other age groups. The onset is usually gradual and the common entrance complaint is swelling and loss of function of an extremity. Systemic manifestations are minimal, though there may be a low grade fever and moderate leukocytosis. These may be the only findings despite multiple sites of involvement. The differential diagnosis includes suppurative arthritis, cellulitis or soft

tissue abscess, scurvy and congenital syphilis.

In some instances the picture is similar to that seen in older children where there is an acute onset with severe systemic manifestations. In these cases it seems that the bacteriemia, which is usually transient, persists and the subsequent course is that of a septicemia. Recovery in such cases is uncommon. In event of recovery from the septicemia the prognosis of the resultant osteomyelitic lesion is unaltered.

Following appropriate treatment in an uncomplicated case the course is benign, characterized chiefly by the rapid healing of wounds and sinus tracts. This usually occurs in from three to eight weeks, though local swelling may persist for a greater period of time and is probably accounted for by extensive formation of involucrum. There is an associated clinical recovery.

Treatment is general as well as local and adequate supportive measures are mandatory. Thus dehydration and anemia are corrected while the affected part is immobilized. Appropriate chemotherapy should be instituted. In some instances no more definitive treatment will be necessary as the osteomyelitis may heal completely. Any subperiosteal or soft tissue abscess must be adequately drained. Adequate immobilization (preferably by a plaster of paris cast) should be continued after the soft tissue abscesses have been drained.

Pyarthrosis is the most common complication and must be differentiated from aseptic serous effusion. For this reason, diagnostic aspiration of the joint is indicated. Epiphyseal separation is the next most common complication and results in residual deformities. Metastatic osseous and soft tissue abscesses are also frequent. Recurrence of the infection and development of chronic osteomyelitis is unusual.

ROENTGEN APPEARANCE

Since the disease runs a relatively benign course the first clinical evidence is usually soft tissue swelling. This may mean that the infection has broken through the

periosteum or into the joint. Roentgenograms in the early stages are rarely obtained. In our experience the earliest finding is an area of bone destruction in the metaphysis adjoining the epiphyseal line. A similar area may be seen in the epiphysis. The periosteum of the diaphysis is elevated. As a result of the effusion the joint space may be widened. Depending on the age of the infant and the affected joint, the epiphysis may not be ossified and its involvement, therefore, cannot be ascertained. On the other hand, the epiphysis may be decalcified or destroyed and only subsequent roentgenograms will show its viability. Partial or complete epiphyseal separation indicates infection of the epiphyseal cartilage.

Healing is evidenced by rapid subperiosteal formation of new bone and by a more discrete limitation of the bony defects and this is followed by restoration of the bony trabeculae. Sequestra are seen rarely; if present, they usually become absorbed. Depending on the extent of epiphyseal destruction there may or may not be restoration of the normal growth.

The course of the disease can be easily followed in the roentgenograms. Complete healing may occur as early as two months with minimal deformities visible for several months. There may be delay in the epiphyseal growth or failure of epiphyseal development with resulting deformities. Sclerosis and other signs of chronic osteomyelitis are uncommon.

There is a great variation in the mortality rate reported in the literature. An example of a high mortality rate is the series reported by Green and Shannon;⁸ 21 per cent of the infants under two years and 44 per cent of those under six months died. Paschlau's¹¹ experience was similar. He reports a mortality rate of 38 per cent in 42 cases under one year of age. Cass,¹ Dillehunt,⁵ and Stone¹⁴ reported an unusually low death rate, probably due to absence of septicemia. In cases with persistent septicemia the comparative prognosis is poor. Thus in those cases in which Green and

Shannon report a positive blood culture the mortality rate was 60 per cent for streptococcus infections and 66 per cent for staphylococcus infections. In infants who survive the septicemia the prognosis of the local lesion is excellent, compared to osteomyelitis in the older age groups.

Because of the unusual number of cases of osteomyelitis in infants in the last year, we would like to report in detail all of the cases which we have seen.

CASE REPORTS

CASE 1. J. M., male (44-10915), aged four weeks, admitted October 27, 1944. Delivery was breech with forceps. On October 1, 1944, numerous small cutaneous pustules were noted. These were opened and treated with sulfathiazole ointment. One week prior to admission, swelling over the right shoulder appeared and three days later similar swellings were seen in the region of the left shoulder, left knee and left ankle. The right shoulder was drained prior to entry. Staphylococci were cultured from the pus.

On admission the baby was undernourished. There was an erythematous eruption over the entire body and swelling over the left shoulder. Both knee joints and the left ankle joint contained increased fluid. Thighs and legs were in flexion and extension provoked pain.

The temperature was 100.8° F., hemoglobin 9 grams and white blood cell count 12,000.

Roentgenograms revealed areas of destruction in the proximal metaphyses of both humeri as well as periosteal elevation (Fig. 1, *A* and *B*). The epiphyseal center on the right was separated. Other areas of destruction were seen in the distal metaphysis and epiphysis of the right femur (Fig. 3*A*), as well as in the upper medial end of the left tibia (Fig. 4*A*). The periosteum was elevated in all instances.

Treatment consisted of two blood transfusions and intramuscular penicillin; 15,000 units were given every three hours for a total of 4,200,000 units. Hospitalization lasted one month during which time the general health of the baby improved markedly.

Progress roentgenograms on November 7, 1944, revealed apparent increase in the bone destruction but roentgenograms taken on November 28, 1944, demonstrated improvement in the appearance of all lesions (Fig. 3*B*). On



FIG. 1. Case I. *A*, November 1, 1944. Destruction of the metaphysis of the right humerus. There are several fragments of necrotic bone. Arrow points to the separated proximal epiphysis. *B*, November 1, 1944. Left humerus: Destruction is less marked. Mild periosteal elevation. Epiphysis shows normal relationship with the metaphysis.

re-examination on January 8, 1945, the lesions appeared well defined on the roentgenograms and there was evidence of healing (Fig. 4*B*). On March 8, 1945, the child appeared clinically well. There was no limitation of motion in any of the involved extremities and roentgenograms showed complete healing (Fig. 2, 3 and 4). The epiphyseal centers in both humeri were not visualized.

Comment. The multiple involvement was secondary to the cutaneous staphylococcus infection. The destruction in both shoulder

regions with epiphysiolysis on the right occurred early and will probably result in permanent deformities. The rapid absorption of sequestra is well demonstrated. It would seem that penicillin had a beneficial influence on the course of the disease.

CASE II. M.-M., female (44-9964), aged two months, admitted September 16, 1944. The infant was breast fed for twelve days until the mother developed a breast abscess. At the age of four weeks the patient developed a temperature of 103°F. and a small area of erythema and

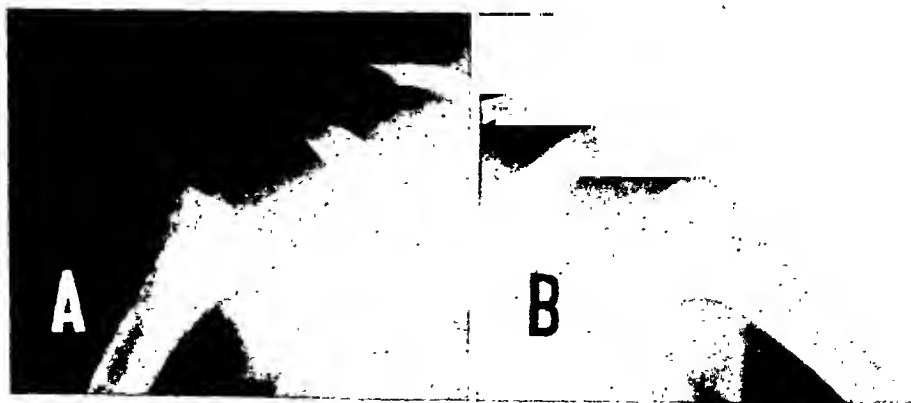


FIG. 2. Case I. *A*, March 12, 1945. Right humerus: The slight irregularity of the metaphyseal outline suggests incomplete healing. The epiphysis has been destroyed. *B*, March 12, 1945. Left humerus: Residual deformity of metaphysis after infection has subsided. Epiphysis has either been destroyed or decalcified.

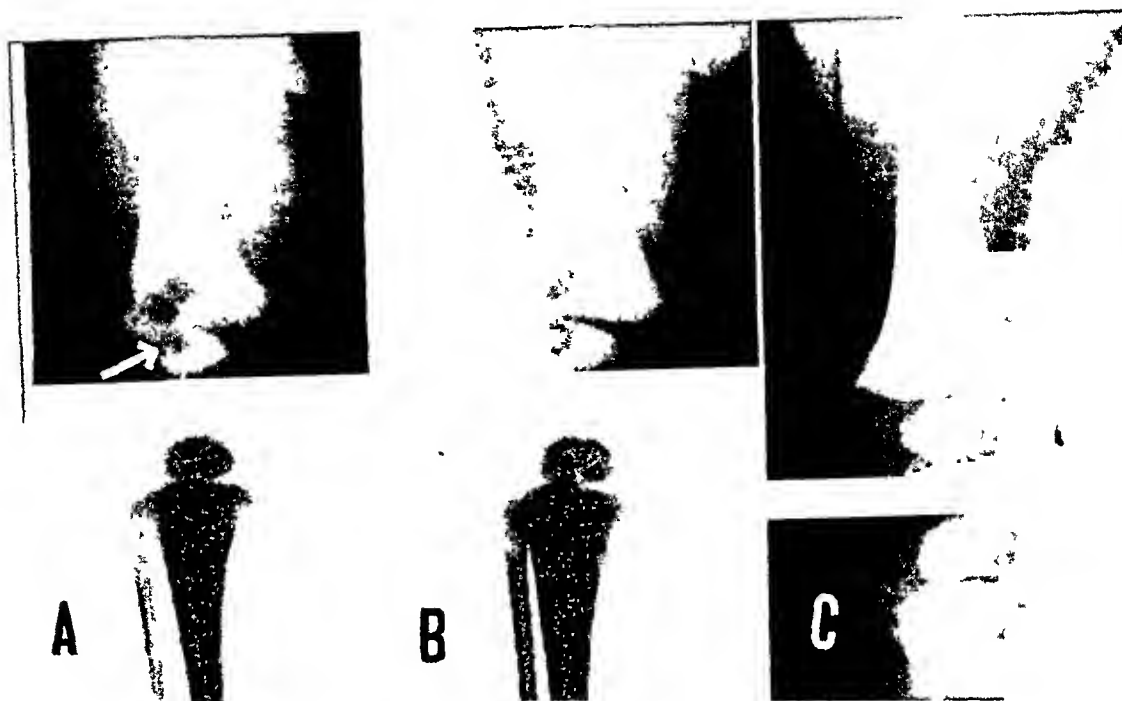


FIG 3. Case 1. *A*, November 7, 1944. Right femur: Circular areas of destruction in the distal metaphysis. Defect in the cortex as well as a rarefied area in the epiphysis (arrow) are well seen. *B*, November 28, 1944. The defects show beginning reossification. Mild periosteal elevation along the lateral femoral aspect. *C*, March 12, 1945. Complete healing in the metaphysis and epiphysis.

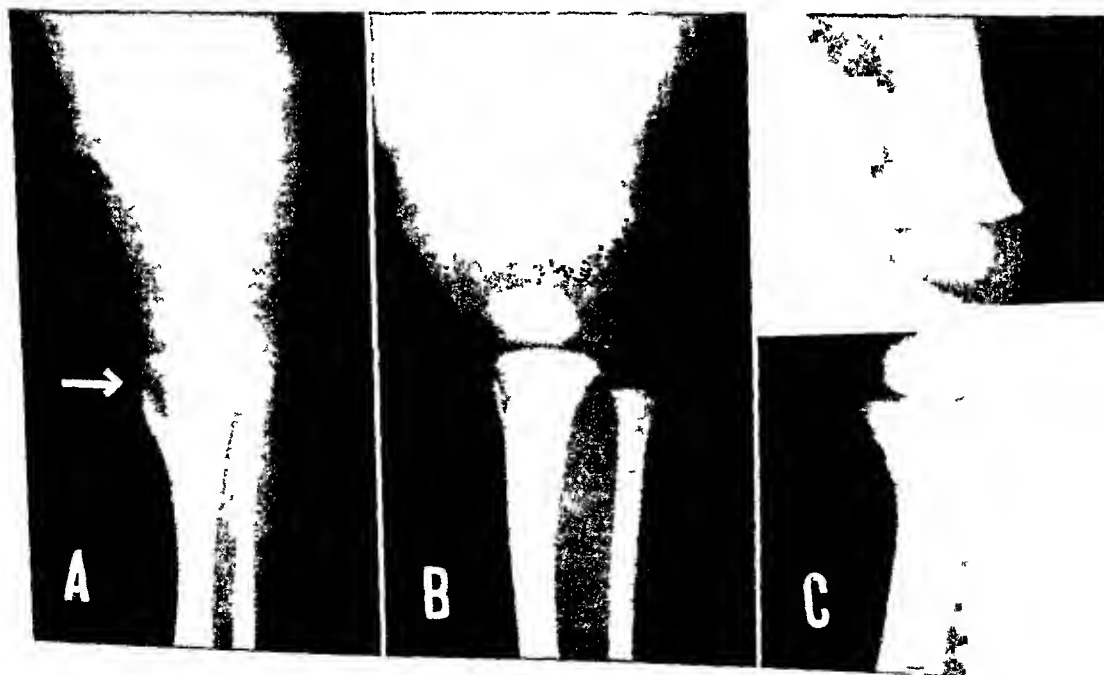


FIG 4. Case 1. *A*, November 7, 1944. Left tibia: Arrow points to break in the cortex from the osteomyelitic abscess in the metaphysis. Slight periosteal elevation. *B*, January 8, 1945. The defect is beginning to fill in with new bone. *C*, March 12, 1945. Complete healing.



FIG. 5. Case II. *A*, September 16, 1944. Area of destruction in the metaphysis. Arrow points to break in the cortex. Some periosteal elevation is present. *B*, April 3, 1945. Complete healing. Normal development of the femur.

swelling over the dorsum of the left fourth finger. Five days later this was incised and pus obtained. Later swelling and tenderness in the region of the right hip was noted. Five hundred thousand units of penicillin were given during the ensuing three weeks. Roentgenograms on September 1, 1944, taken in another hospital, revealed effusion into the right hip joint and roentgenogram on September 13, 1944, showed destruction of the head of the femur.

On admission the infant appeared chronically ill. There was swelling in the region of the left fourth finger. Movement of the right thigh was painful.

Temperature was 99.4° F., hemoglobin 10.8 grams and white blood cell count 24,000.

Roentgenograms revealed an irregular area of bone destruction in the proximal right femoral metaphysis and mild periosteal elevation (Fig. 5*A*). There was marked destruction in the proximal phalanx of the left fourth finger and several sequestra were seen (Fig. 6*A*).

Treatment consisted of application of a single hip spica plaster of paris cast and 10,000 units of penicillin every three hours for a total of 400,000 units. The infant remained afebrile and improved during her hospital stay. Drainage from the hand gradually subsided. October 10, 1944, a sequestrum was removed from the left fourth finger.

On April 3, 1945, there was complete healing of the femoral lesion without limitation of

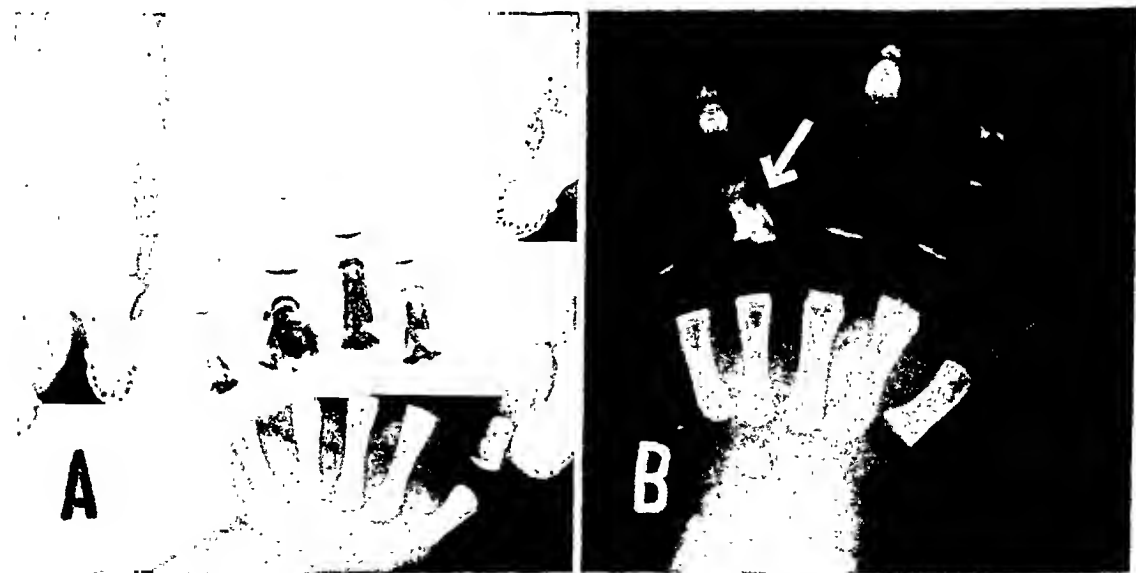


FIG. 6. Case II. *A*, September 16, 1944. Extensive destruction of the proximal phalanx of the fourth finger. Several sequestra are seen. *B*, April 3, 1945. Arrow points to a small cavity containing a minute sequestrum. The outline of the phalanx is smooth.

motion (Fig. 5B). The left fourth finger revealed a small abscess cavity with a minute sequestrum (Fig. 6B).

Comment. It is interesting to consider the possible relationship between the mother's breast abscess and the patient's infection. The infection in the upper extremity was farther advanced than in the lower extremity. Penicillin seemed helpful in pro-

Roentgenograms revealed a circular area of destruction in the lower femoral metaphysis and periosteal elevation (Fig. 7A).

Treatment consisted of aspiration of the knee joint. A cloudy fluid was obtained which was negative on culture. Five thousand units of penicillin were injected into the knee joint and the procedure was repeated on two consecutive days. On August 11, 1944, the abscess in the left femur was drained. The knee joint was

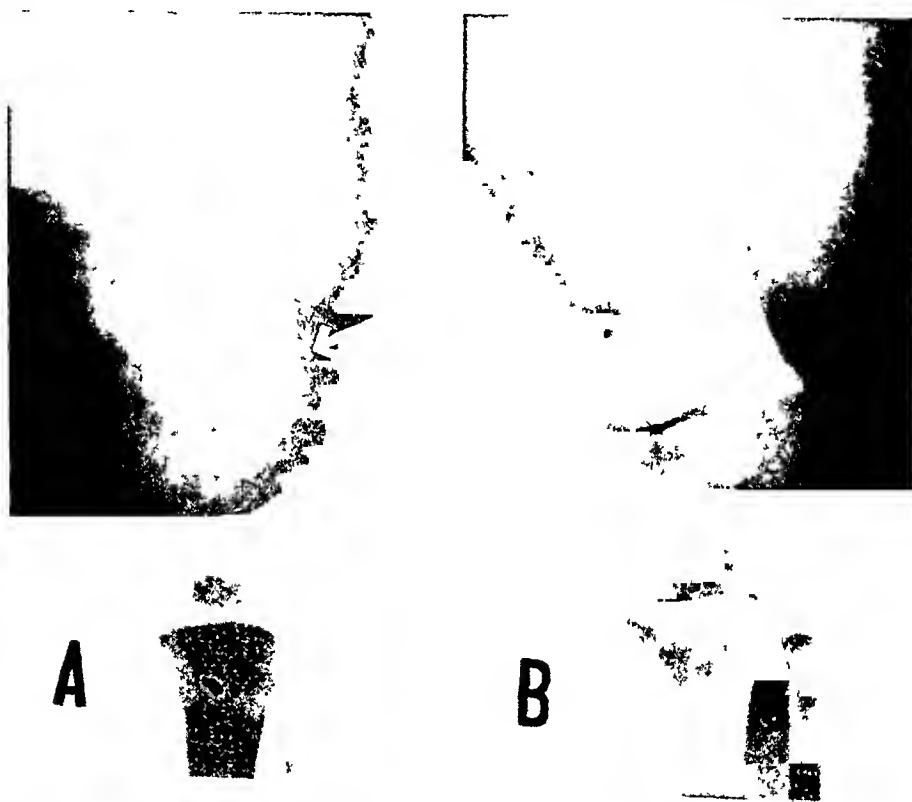


FIG. 7. Case III. A, August 11, 1944. Circular area of destruction in the lower femoral metaphysis. Moderate amount of periosteal elevation. B, March 26, 1945. Complete healing and normal growth of bone.

ducing the satisfactory outcome. This is the only case in which a sequestrectomy was performed and in which there is a persisting sequestrum.

CASE III. J. E., male (44-6368), aged five weeks, admitted August 2, 1944. Three days before admission the parents noticed swelling of the left knee. The temperature was normal but the infant was irritable. Previous medical history was not significant.

On admission examination was negative except for swelling of the left knee.

Temperature was 99° F., hemoglobin 12 grams and the white blood cell count 11,200.

opened simultaneously and about 30 cc. of thick, creamy pus was liberated. Following this a single hip spica plaster of paris cast was applied. Intramuscular penicillin, 10,000 units every four hours, was begun on August 11, 1944, and continued until August 17 for a total of 600,000 units.

The cast was removed on October 20, 1944, at which time the wound had healed and full range of motion was present. The child was clinically well.

At the last examination on March 26, 1945, the roentgenograms showed complete healing of the lesion and there was no impairment of motion of the knee joint (Fig. 7B).

Comment. This infant had the shortest duration of symptoms of any of the cases seen by us. Penicillin given intramuscularly and into the knee joint probably attenuated the virulence of the infection. In spite of the extensive pyarthrosis—as proved at operation—there was no apparent residual impairment in the function of the joint.

CASE IV. C. W., male (44-6176), aged three and one-half weeks, admitted June 28, 1944. Delivery was normal. Swelling of the right thigh was noted on the thirteenth day. This appeared painful on palpation and movement and the infant kept the leg flexed. Hot packs were applied until an area of fluctuation appeared over the lateral aspect of the lower right femur. Three days before admission this area was incised and drained.

On admission, examination was normal save for a small draining sinus in the region of the right knee. The thigh was swollen and indurated and the leg was held in flexion.

Temperature was 99.5° F., hemoglobin 11 grams and the white blood cell count 20,400.

Roentgenograms showed an area of destruction in the distal femoral metaphysis with peri-

osteal elevation. The distal femoral epiphysis appeared normal (Fig. 8A).

Treatment consisted of intramuscular penicillin. Ten thousand units were given every four hours for a total of 600,000 units. On July 11, 1944, the soft tissue abscess in the region of the external femoral condyle was adequately drained. A chronic abscess cavity was found which communicated with the knee joint. The perforation into the joint was enlarged and about 10 cc. of thick, yellow pus was liberated, which was negative on culture. Vaseline gauze was loosely packed into the defect and a single hip spica plaster of paris cast and applied. The temperature remained normal and the general condition was good. When the cast was removed on August 16, 1944, the wound appeared to be healing (Fig. 8B). There was full range of motion in the knee joint.

At the last examination on January 12, 1945, roentgenograms revealed progressive healing of the defect. Only a minimal deformity in the metaphysis was present (Fig. 8C). The bone growth was normal and there was no limitation of motion.

Comment. Course and treatment are similar to Case III. Of interest is the un-

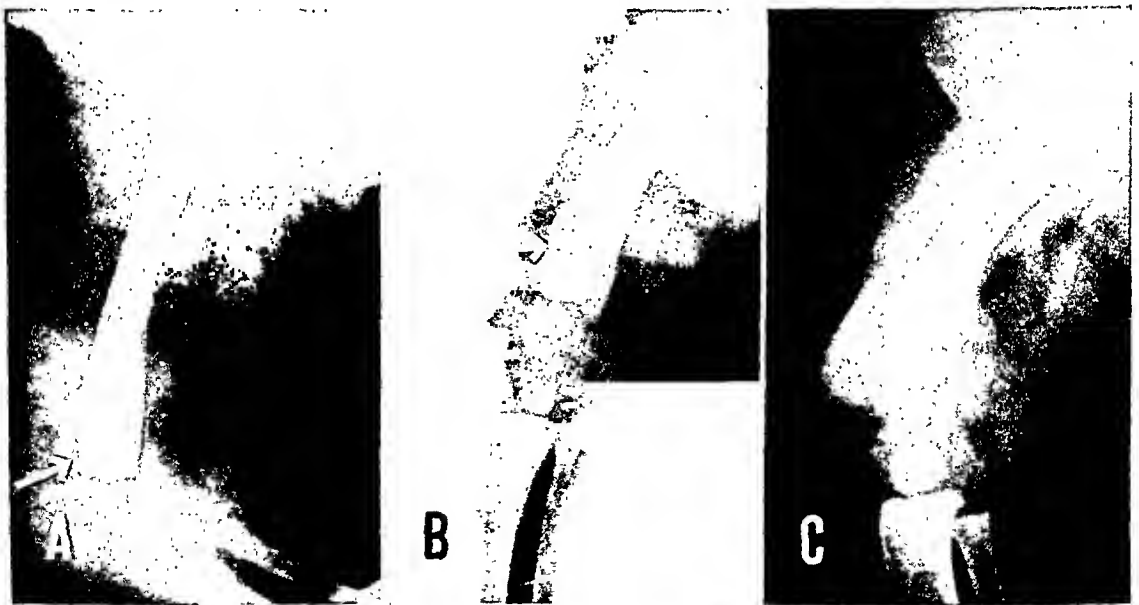


FIG. 8. Case IV. A, July 10, 1944. Area of destruction in the lower femoral metaphysis. Arrow points to break in cortex. Moderate amount of periosteal elevation. B, August 16, 1944. Healing progresses, while the femur grows normally. C, January 12, 1945. Only a mild deformity remains in the posterior aspect of the metaphysis.

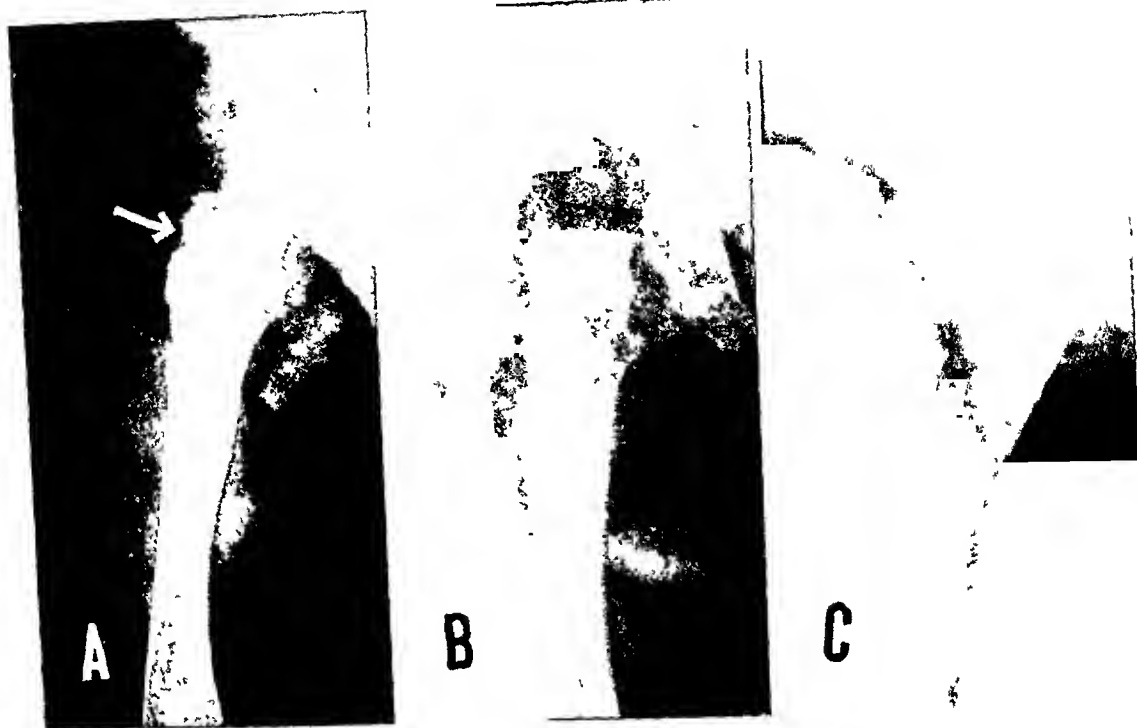


FIG. 9. Case v. *A*, June 12, 1941. Several areas of destruction in the metaphysis. Arrow points to break in the cortex. Moderate amount of periosteal elevation. *B*, August 11, 1941. The infection appears healed. *C*, April 7, 1943. Normal bone growth without residual deformity.

disturbed enchondral growth of bone in the presence of the metaphyseal abscess and involvement of the epiphysis—as demonstrated at the time of operation.

CASE V. L. O., male (41-6896), aged five months, admitted June 12, 1941. Previous medical history was not significant. Swelling in the right hip region was noted at the age of two months. There was an associated febrile reaction. After immobilization for three weeks the hip region was incised and drained. Culture revealed pneumococci. The leg was placed in skin traction.

Examination on admission revealed a normally developed infant. The right thigh was in 20° flexion. Movement in the hip joint was free but painful. There was a small amount of purulent drainage from the wound.

Temperature was 99.6° F., hemoglobin 13.5 grams and the white blood cell count 17,500.

Roentgenograms revealed several well defined areas of destruction in the proximal femoral metaphysis as well as mild periosteal elevation. The capital epiphysis appeared normal (Fig. 9*A*).

Treatment consisted of immobilization in a one and a half hip spica plaster of paris cast for three months at which time the wound had healed and the child was clinically well.

Progress roentgenograms showed healing of the lesion (Fig. 9*B*) and the last taken on April 7, 1943, showed normal development of the right femur (Fig. 9*C*). Examination at that time revealed no limitation of motion.

Comment. The culture of pneumococci suggests an upper respiratory tract infection for the port of entry. The infection was subsiding when we saw this infant. Adequate treatment had been given early and no deformities resulted.

CASE VI. L. M., female (41-11698), aged six and one-half months, admitted March 22, 1942. The child was adopted at the age of three and one-half months and was in good health until the age of four and one-half months when swelling over the right ankle was noted. The area was painful and tender. Temperature was 101° F. and a roentgenogram was said to be negative. Sulfathiazole was administered with

relief of symptoms. At six months the symptoms recurred and were not influenced by sulfathiazole.

On admission the child was normally developed. There was moderate swelling of the entire right thigh and leg with induration over the right ankle. Movement of the leg was painful.

Temperature was 100.2° F., hemoglobin 9.5 grams and the white blood cell count 13,800.

the entire right femur and an area of destruction was seen in the proximal femoral metaphysis (Fig. 10C). The capital epiphysis appeared normal. The white blood cell count at that time was 16,200. Aspiration of the hip joint yielded no pus. Immobilization was continued. Progress roentgen studies revealed gradual healing of the tibial and femoral lesions. The last roentgenogram on November 10, 1944, showed complete healing (Fig. 11). Examina-



FIG. 10. Case VI. *A*, March 23, 1941. Extensive periosteal elevation of the tibia. No definite metaphyseal focus is seen, but there is some irregularity in the distal tibial metaphysis. *B*, March 23, 1941. Arrow points to infraction in the subperiosteal new bone and tibia. Note the periosteal elevation in the lower femur and the normal appearance of the proximal femoral region. *C*, May 12, 1942. There is now destruction in the proximal femoral metaphysis (arrow) and further extension of the periosteal elevation.

Roentgenograms revealed extensive periosteal elevation involving the entire right tibia and lower portion of the right femur. Infraction through the new bone and old cortex was seen in the anterior aspect of the tibia. The distal tibial metaphysis had a moth-eaten appearance (Fig. 10, *A* and *B*).

Treatment consisted of immobilization in a hip spica plaster of paris cast. A progress roentgenogram on May 11, 1942, revealed improvement in the appearance of the tibia. There was, however, periosteal elevation involving

tion at that time showed equal development of both lower extremities and free movement of all joints.

Comment. The extensive periosteal reaction most marked in the distal tibial region was not observed in any of the other cases. It is similar to a case reported by Grevillius.⁹ This case demonstrated the remarkable ability of the infant's skeletal system to combat infection and return to an essentially normal architectural structure.

CASE VII. C. S., male (40-9254), aged seven months, admitted July 14, 1940. Umbilical infection developed after birth with purulent discharge lasting for eight weeks. At the age of three weeks the infant was said to have had pneumonia. Swelling in the left shoulder region was noted at the age of six weeks. This was drained one week following onset with liberation of about 4 cc. of pus. Drainage subsided after several days with healing of the wound.

On admission the temperature was 100.4°F. , and the infant was normally developed. The left arm was held in adduction. Abduction and internal rotation were limited and painful. There was no soft tissue swelling.

Roentgenograms of the left shoulder revealed absence of the epiphysis and destruction in the metaphysis with a sequestrum (Fig. 12*A*).

Treatment consisted of immobilization in abduction. Roentgenograms showed progressive healing with persisting deformity of the proximal end of the humerus. He was well until March, 1943, when he was readmitted with a soft tissue abscess in the posterior aspect of the upper arm. The systemic reaction was minimal. The abscess was drained and culture revealed a non-hemolytic streptococcus. Roentgenograms showed no change over those taken previously. On his last visit on February 4, 1944, there was limitation of motion with a 30° abduction, good internal rotation but no external rotation. Roentgenograms showed absorption of the sequestrum and some sclerosis of the shaft. Two epiphyseal centers of the proximal humerus were present (Fig. 12*B*).

Comment. The focus of the infection could have been the omphalitis but the upper respiratory infection was a more likely cause. The sequestrum was absorbed gradually.



FIG. 11. Case VI. November 10, 1944. Complete healing of the lesions in the right lower extremity. Normal bone development.



FIG. 12. Case VII. *A*, July 13, 1940. Destruction of bone in the proximal humeral metaphysis with circular sequestrum in the center of the shaft (arrow). No epiphyseal center is seen. *B*, March 18, 1943. Residual humerus are visible. Sclerosis of the shaft.

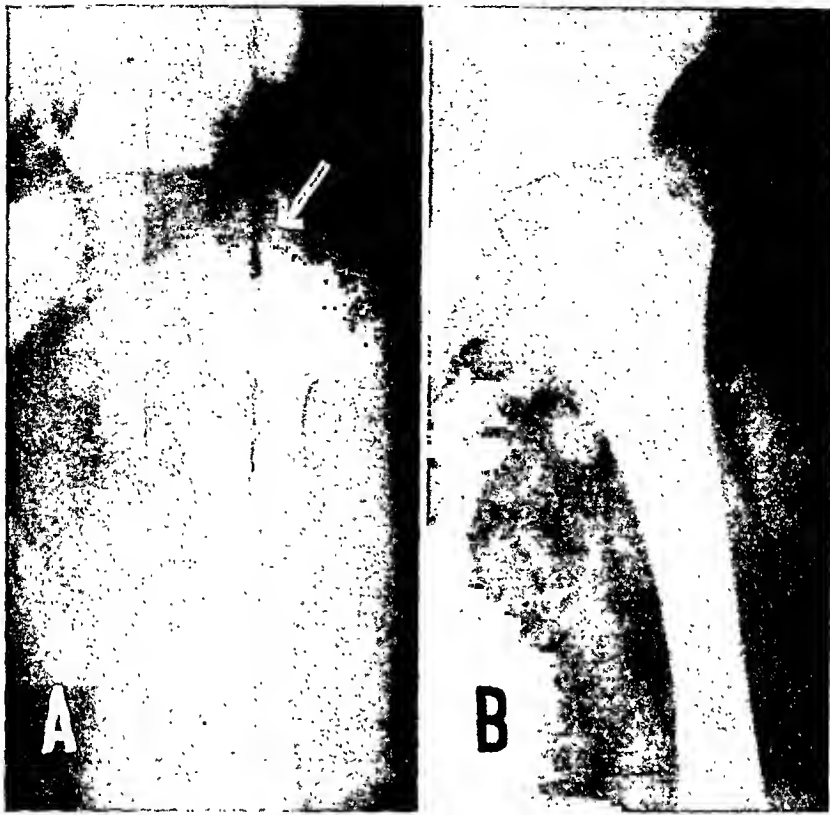


FIG. 13. Case VIII. *A*, April 19, 1944. Widening of the joint space, area of destruction in the metaphysis (arrow) and periosteal elevation. The epiphysis is barely visible and appears partly decalcified. *B*, August 18, 1944. Metaphyseal outline is smooth and the joint space is of normal width. The epiphyseal center has disappeared.



FIG. 14. Case VIII. November 16, 1944. Residual instability and subluxation in the left hip.

ually over a period of nearly three years. The sclerosis of the humeral shaft indicates a chronic osteomyelitis. This is the only case in which the course of the disease was similar to that seen in the older age groups.

CASE VIII. R. K., male (44-3824), aged nine months, admitted April 19, 1944. At the age of six months the child developed a protracted upper respiratory infection complicated by otitis media. Pneumonia developed at six and one-half months and at that time swelling and redness over the left hip joint were noted. Sulfadiazine was given and the child became afebrile but the extreme tenderness and swelling remained. On March 16, 1944, an incision was made in this area but no pus was obtained. Subsequently the swelling decreased slightly but the tenderness remained. The temperature was elevated only occasionally.

On admission the hip was held in 110° flexion and 90° external rotation. Motion was free but painful. The incision was healed. The general condition was good.

Temperature was 102.4° F., hemoglobin 11 grams and the white blood cell count 17,500.

Roentgenogram showed subluxation of the left hip, an area of destruction in the metaphysis and periosteal elevation. The epiphyseal center was small and irregular (Fig. 13A).

Treatment consisted of a hip spica plaster of paris cast for two months followed by a brace. Progress roentgenograms revealed healing in the metaphysis (Fig. 13B). The epiphysis was not visible on November 16, 1944 (Fig. 14). Flexion of the hip was limited to 30° , abduction to 15° and adduction to 35° . The child was clinically well.

Comment. This case demonstrates the rule that pyarthrosis commonly occurs when the osteomyelitis develops in the proximal femoral metaphysis. Of interest is the speed of the complete dissolution of the head of the femur.

CASE IX. T. P., male (39-92), aged seven months, admitted January 13, 1939. The infant had diarrhea at the age of three weeks followed by pneumonia at two months. Two weeks later swelling of the right thigh was noted. This was incised and pus was obtained.

On admission the child was undernourished. The entire right thigh was swollen and pus

exuded from two rubber drains. The thigh was held in flexion. There was pain on extension.

The temperature was 98° F., hemoglobin 10 grams and white blood cell count 11,460.

Roentgenograms showed an irregular area of destruction in the roof of the acetabulum and periosteal elevation of the femur. The capital epiphysis was not visible.

Treatment consisted of adequate drainage and immobilization. Progress was satisfactory



FIG. 15. Case IX. April 15, 1941. Final roentgenogram showing a shallow acetabulum with an oblique and irregular roof. Subluxation of the hip with absence of the femoral epiphysis.

with gradual healing of the sinus. Follow-up roentgenograms showed a shallow acetabulum with subluxation of the femur. The last roentgenograms on May 20, 1943, revealed absence of the capital epiphysis (Fig. 15). The child walked with a limp. Limitation of motion in the hip joint was present and there was a shortening of 1 inch.

Comment. An upper respiratory infection was again the source of the infection. The rapid destruction of the bony tissue about the hip was demonstrated in this case—four months after the onset.

CASE X. J. P., male (J-1667), aged six months, admitted February 23, 1934. Early medical history was not significant. At the age of four and



FIG. 16. Case x. April 17, 1935. Final roentgenogram showing bilateral deformities of the acetabula. On the left there is destruction of the epiphysis and subluxation. The small shadow adjoining the metaphysis on the right may be delayed development of the epiphysis.

one-half months the infant developed high fever and enlarged cervical lymph nodes. One week later it was noted that he held both thighs in flexion and splinted the left arm. The left shoulder area was drained in a local hospital. A week later the right hip region was opened and a large amount of pus liberated. Additional areas of swelling in the left side of the neck, right wrist, right axilla and left hip were drained. Paracentesis for left otitis media was performed.

On admission pus could be expressed from sinuses in both hip regions. The remaining wounds were healed. The infant had bilateral otitis media.

Temperature was 102° F., hemoglobin 8 grams and the white blood cell count was 38,100. Blood culture was negative.

Roentgenograms revealed normal shoulder and wrist joints. There was destruction in both acetabula, more marked on the right side, with loss of the capital epiphysis and mild destruction in the proximal portions of both femoral metaphyses. The hip joints were subluxated.

The left hip joint was drained on March 2, 1934, and a large amount of pus liberated. Traction was applied to both lower extremities.

Temperature gradually returned to normal and drainage ceased within the month.

Progress roentgenograms showed gradual healing. Final roentgenograms on April 17, 1935, revealed deformities of the acetabula with destruction of the capital epiphysis on the left. A small capital epiphysis was seen on the right (Fig. 16). At that time all joints were freely movable. The gait, however, was unsteady.

Comment. Presumably the focus of infection was in the upper respiratory tract. The infant developed numerous metastatic abscesses involving apparently only the soft tissues with the exception of both hip regions. Bilateral hip involvement is unusual. The destruction was more extensive on the left. The appearance of the right capital epiphysis was delayed.

DISCUSSION

It is generally accepted that osteomyelitis in infants has a different course than in older age groups. It is difficult, however, to fix the age at which this change occurs. We

selected infants in whom the illness began before they reached the age of six months, while other observers have included infants up to one or two years of age. There is, however, definite indication that with the advancing age of the infant the disease will resemble more and more the infection in older children. In our series the infections were relatively benign and the pathologic changes were often reversible if the diagnosis was made early and adequate treatment instituted.

Other authors have stressed the higher incidence of streptococcus infections in infants. Our series does not offer sufficient bacteriologic data to be significant, as the primary drainage was carried out elsewhere in many cases. In 2 instances in which penicillin had been given the cultures were negative.

Certain anatomic factors in the infant allow early natural decompression of the metaphyseal abscess, either into the subperiosteal space or the neighboring joint. The latter usually depends upon the joint which is involved. It may be difficult to retrace the course of the infection when the joint is involved at the time of the first examination. The possibility of primary suppurative arthritis must occasionally be considered. When Cases ix and x were first seen in our hospital they revealed destruction of the capital epiphyses, acetabula and metaphyses. The clinical and roentgenographic courses, however, were similar to those in other cases and we believe that the infection was primarily an osteomyelitis.

Six of our 10 cases had a history of upper respiratory, umbilical or cutaneous infection, while the mother of one had a breast abscess. These observations are in accord with those of others who described similar infections accounting for the bacteriemia and subsequent osteomyelitis.

Local swelling and malfunction of an extremity were usually the first signs. Systemic manifestations were minimal, even though in several cases the lesions were multiple at the onset. Rapid improvement

occurred after decompression of the soft tissue abscesses. Drainage from the abscesses subsided within three to twelve weeks.

The earliest roentgenograms revealed areas of rarefaction in the metaphyses. Periosteal elevation was usually present. In some cases, healing of the lesions was noted on admission. In all cases, the roentgenograms offered an excellent opportunity to study the course of the infection.

Destruction of the epiphyseal cartilage, epiphyseal center and cartilage of the joint seems to be the most common and most serious complication, as it is followed by a disturbance of growth of enchondral bone with ultimate deformity. A persisting sequestrum was seen in only 1 case.

Treatment consisted of immobilization and supportive measures. Drainage of one or more abscesses was performed in 8 cases. In no instance was a direct surgical attack upon the bone necessary for drainage. One case received penicillin and another sulfonamides without surgical interference. Drainage was combined with chemotherapy in 4 patients. The small number of cases does not allow us to draw conclusions regarding the type of chemotherapy which promises better results. We believe that all soft tissue abscesses should be drained early and that penicillin should be administered. In cases with associated suppurative arthritis early drainage will minimize the destruction of the joint. In addition, all affected extremities should be immobilized and supportive measures instituted.

SUMMARY

1. Ten cases of osteomyelitis in infants under six months of age are reported.
2. The benign course of the disease and its differences from the disease in older children are emphasized. The pathologic process was reversible in several cases and the clinical recovery in all cases was complete.
3. Roentgenograms are invaluable in detecting the presence of the disease, in following its different phases and in evaluating the end-results.

4. Involvement of a joint is common and is the most serious complication.

5. Good treatment consists of: (a) supportive measures; (b) early, adequate drainage of the soft tissue abscesses; (c) immobilization; (d) chemotherapy.

The authors are indebted to Dr. H. D. Kerr and Dr. J. W. Dulin for their valuable suggestions in the preparation of this paper.

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THE OCCASIONAL APPEARANCE OF BOTH INNER AND OUTER SUTURE LINES IN ROENTGENOGRAMS OF THE SKULL SIMULATING FISSURE FRACTURE

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THE anatomical fact of the existence of separate suture lines for the outer and the inner tables of the calvarium has been given comparatively little consideration in the roentgenological, surgical and anatomical literature. Since it has led to the erroneous diagnosis of fissure fracture of the skull, it is worthy of discussion. Many textbooks on roentgen diagnosis, including those dealing exclusively with roentgen diagnosis of the skull and diagnosis of fractures, fail to mention this anatomical detail. No specific paper dealing with this subject was discovered in the literature of

the last decade; however, illustrations with correct description of the double suture line have been published by Dyke^{1,2} and by Schwartz.^{5,6}

Analysis of illustrations of the calvarium in anatomical textbooks such as in Spalteholz' "Hand Atlas of Human Anatomy,"⁷ reveals a surprising difference in the appearance of the two sutures. The sutures of the inner table form comparatively straight lines while the sutures of the outer table present the well known serrated appearance. This difference is equally well demonstrated on the specimen of a skull (Fig. 1,

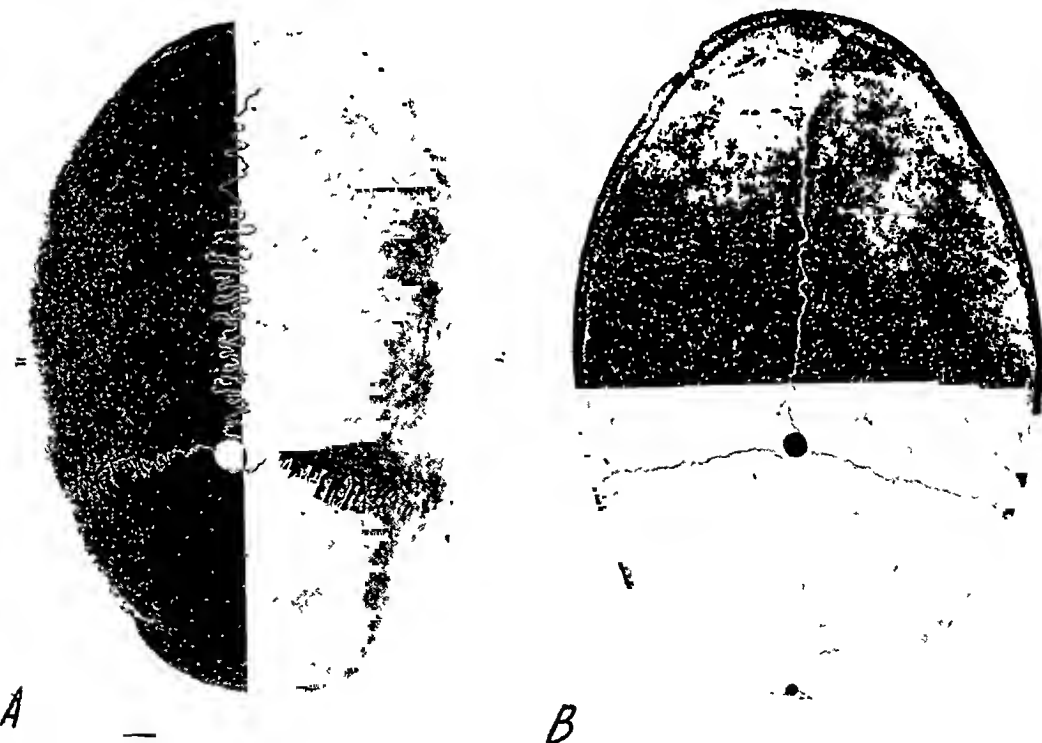


FIG. 1. A, normal dried specimen viewed from the outer surface demonstrating the serrated external suture lines. B, photograph of the inner surface showing the comparatively straight internal sutures.



FIG. 2. Roentgenogram of the same skull photographed in Figure 1, showing "double suture lines" in the sagittal and right coronal sutures.

A and *B*). A roentgenogram of the same dried specimen (Fig. 2) shows both suture lines superimposed with the straight sutures of the tabula interna crossing the meanderings of the external suture lines.

In routine skull roentgenograms this "double suture line" is most frequently seen in the sagittal suture and the medial portions of the coronal and lambdoid sutures. It may appear in other sutures and is not necessarily symmetrical. It is most clearly demonstrated where there are other sutural variations, such as the persistent frontal (metopic) suture.

The illustrations (Fig. 3, *A* and *B*) show these double lines in a patient with no history of any previous injury to the skull. The roentgenogram reproduced in Figure 4. *A* was taken following an epileptic attack and diagnosed at another hospital as a

"linear fracture of the anterior portion of the left parietal bone." In this department the suspected line was considered to be a double suture line; this interpretation is given added strength by the demonstration in the same patient of another double suture line along the sagittal suture (Fig. 4*B*).

In personal discussions with competent specialists in various fields, lack of familiarity with this anatomical curiosity was



FIG. 4. *A*, erroneous diagnosis of "fissure fracture of the skull" in a case of double suture lines of the coronal suture. *B*, demonstrating the presence of double lines over the sagittal suture of the same patient.

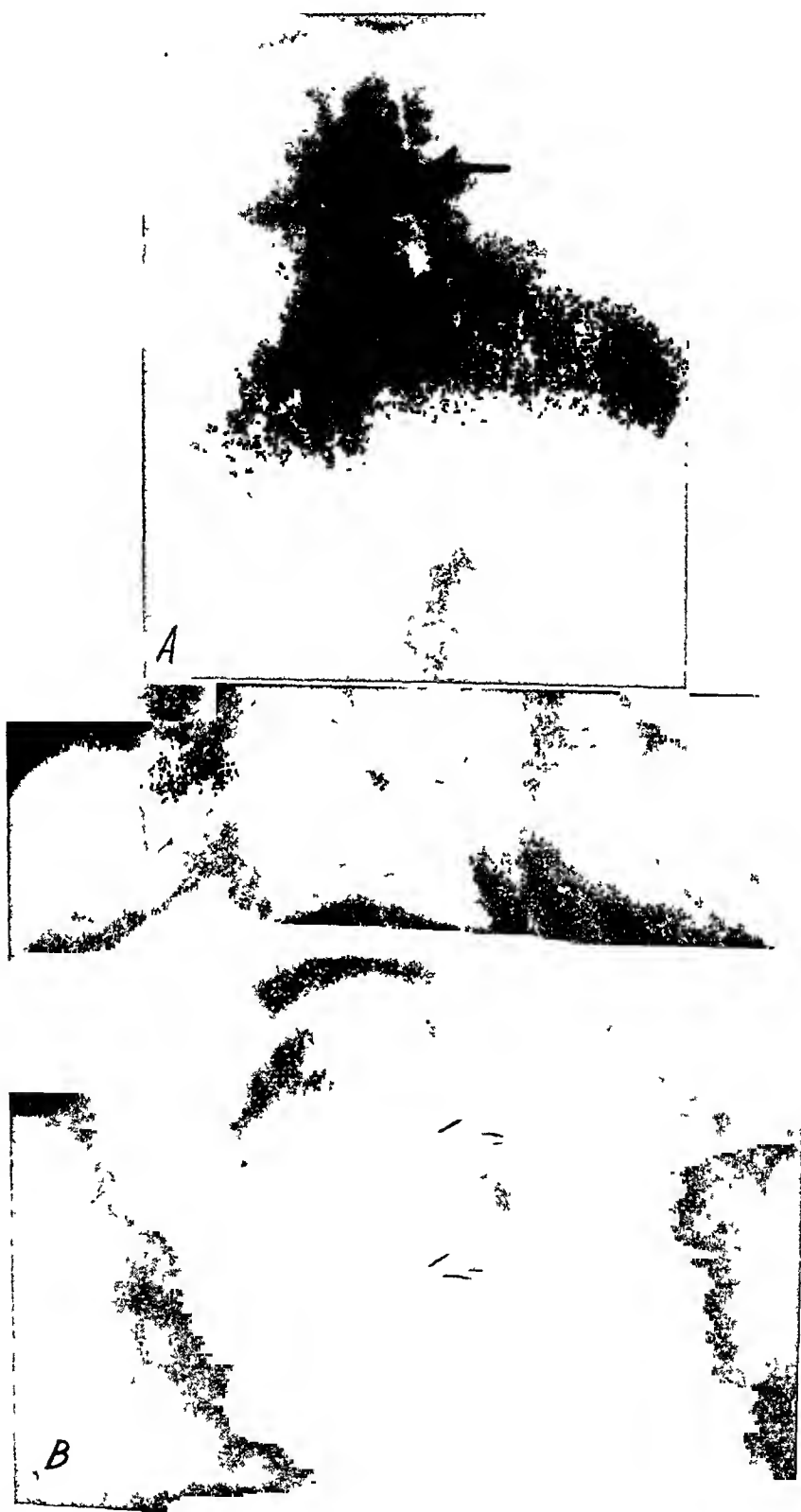


FIG. 3. *A*, double lines of the sagittal suture seen in the anteroposterior projection. *B*, demonstrating the same lines in the submentovertical base projection.

evident. Again repeated erroneous diagnosis of fissure fracture of the skull based on roentgenological demonstration of these double lines was encountered. Therefore it seems appropriate to re-emphasize this anatomical relationship in order to avoid diagnostic errors.

CONCLUSIONS

1. Anatomical and roentgenological illustrations demonstrating the phenomenon of the "double suture lines of the skull" are presented.

2. The origin of these double lines is analyzed as being caused by the superimposition of the comparatively straight inner sutures upon the serrated outer suture lines.

3. A warning is issued against the erroneous diagnosis of a "fissure fracture of the skull running along the suture" and a pertinent case is illustrated.

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DUPLICATION OF THE ENTIRE LARGE INTESTINE (COLON DUPLEX)

REPORT OF CASE*

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EARLY in October, 1944, a healthy looking, rather corpulent young woman was referred by a medical consultant of the Mayo Clinic to the Section on Roentgenology for examination of the large intestine. The consultant noted only that she had been suffering from obstipation. Proctoscopic examination performed the day before had revealed that the rectum and lower portion of the sigmoid colon were normal except that they were displaced markedly toward the right side by what was thought to be a mass in the left side of the pelvis.

Preliminary roentgenoscopic inspection of the abdominal field revealed nothing abnormal. After the contrast enema was begun, it was evident that the rectum was displaced toward the right side and the dim outline of a pelvic mass could be seen. No other roentgenoscopic evidence of intestinal abnormality was elicited. Postero-anterior and anteroposterior roentgenograms of the abdomen were made after the patient had expelled the bulk of the contrast enema (Fig. 1). Immediately thereafter the colon was redistended with air in an attempt to determine more adequately the anatomic relation of the pelvic mass to the rectum and sigmoid (Fig. 2a). A diagnosis of duplication of the entire colon was made.

The supernumerary colon, which contained a material impervious to roentgen rays, was visible on the roentgenograms. We were and still are convinced that the material in the supernumerary colon was

not a part of the contrast enema because its concentration was so uniform throughout, and because the lumen containing it could be shown to communicate neither with the normal colon nor with the outside of the body. Since the excretion of calcium occurs chiefly through the mucous membrane of the large intestine, we reasoned that the opaque element in this material was calcium, and that it was concentrated in the anomalous colon because the mucous membrane retained its function of excreting calcium even without a channel through which to eliminate it. The extra colon had a well formed rectal ampulla and sigmoid loop. Its course ran parallel to that of the normal colon throughout; the rectal, sigmoidal, descending, cecal, and ascending portions lay lateral to, and the transverse portion above, the analogous normal portions (Fig. 2b). The anatomic relationship of the two lumens was obviously intimate. Along the inferior border of the lumen of the normal colon a short crescentic deformity was visible (Fig. 1 and 2a). The cause of this was not determined pre-operatively, but after the operation we decided that it was probably a site of reaction in the region where surgical drainage had been instituted elsewhere before the patient came under our observation.

The patient was a married woman, aged twenty-seven, who since the first week in September, 1944, had been having attacks of sharp pain across the lower part of the abdomen accompanied by obstipation. The obstipation was

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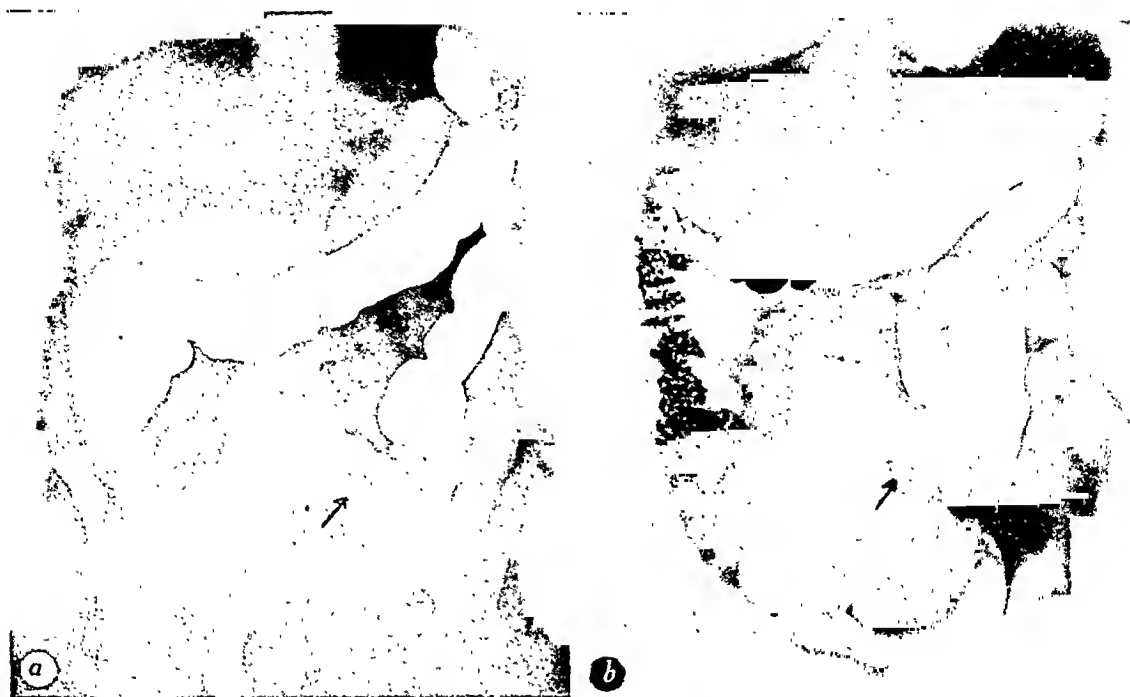


FIG. 1. *a*, anteroposterior and *b*, posteroanterior roentgenograms of the colon after the contrast enema was expelled. The denser shadow is the normal colon showing the rectum displaced toward the right side and the sigmoid colon elevated by the pelvic mass made up of the ampulla of the extra rectum and sigmoid colon. The arrows point to the crescentic deformity referred to in the text. The course and contour of the duplicated colon are best shown in *a*.

so severe that emptying of the intestine was accomplished only with the use of enemas. On one occasion she took a laxative which did not relieve the pain she was having although it did promote defecation. Two days later her temperature rose to 107° F. and she had chills. The patient was taken to a hospital, was given fluids by the intravenous route and a hypodermic injection of a sedative. Her temperature returned to normal after a short interval. During the attacks the patient noticed much rumbling in the abdomen. She was always able to pass gas by rectum but she was never able to pass feces without the use of enemas. She also noticed that it was becoming progressively more difficult for her to expel enemas, chiefly because the abdominal pain and cramps were increasing steadily in severity. Blood was never noticed in the stool. The patient had been nauseated but she had never vomited. In the final six weeks before registration at the Clinic she had lost 20 pounds (9.1 kg.).

There had been several similar attacks of abdominal difficulty before the onset of this series of events. The patient was seen at the Clinic in 1919 when she was eighteen months old. At

that time congenital dislocation of the right hip was reduced successfully by manipulation and application of a double spica cast. In 1921, when the patient was three years old, she was operated on elsewhere for acute intestinal obstruction. The surgeon relieved what he called a "kink" in the region of the sigmoid flexure and created an opening into what he thought at the time was the colon but which he subsequently came to believe was a mesenteric cyst. In 1937, when the patient was about nineteen years old, the same surgeon operated on her again, this time for acute appendicitis. He removed two appendices, both from the tip of the cecum, one of which was gangrenous. The abdomen was not explored at that time because of the acute inflammatory condition of the appendix. Three years later, in 1940, the same surgeon explored the abdomen, this time because of symptoms of partial intestinal obstruction. He tried unsuccessfully to remove what he thought was the mesenteric cyst so he again drained it. Recovery was satisfactory, but a cutaneous fistula which opened and closed at intervals persisted in the abdominal scar. When draining, it usually yielded serous fluid but

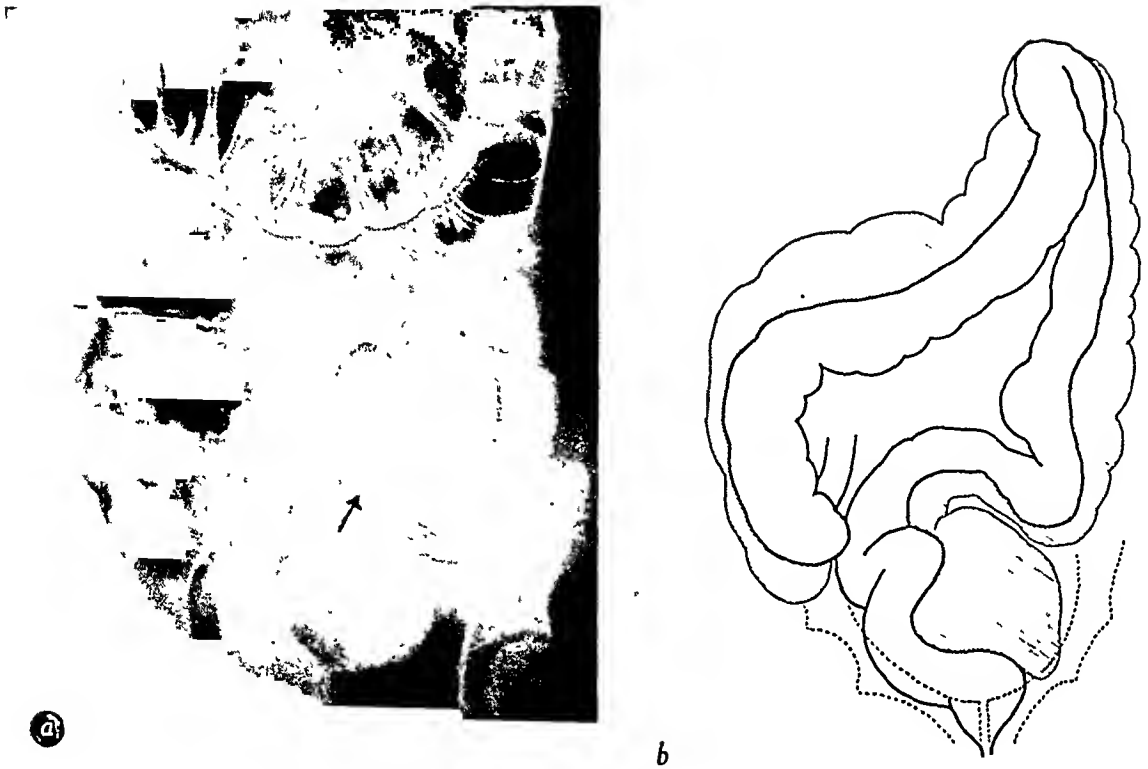


FIG. 2. *a*, anteroposterior roentgenogram of the colon after redistention with air. The duplicated colon is not clearly shown but the distention of the normal colon is well shown. The arrow points to the crescentic deformity referred to in the text. *b*, Diagrammatic interpretation of the roentgenograms.

there were times when gas and liquid feces emerged through the opening. In other respects the patient remained well until the renewed onset of symptoms in 1944 when the surgeon observed an enlarging pelvic mass.

The patient gave a normal menstrual history. In a letter to the Clinic the surgeon noted that the patient had a double uterus and double cervix, and that she had had two early miscarriages. Her husband, twenty-five years of age, was living and well. The family history revealed nothing pertinent.

Physical examination revealed a well developed, somewhat obese woman in apparent good health. The temperature was 98.2° F. The systolic blood pressure was 130, the diastolic 90 mm. of mercury. The breasts were normal. Several abdominal scars were noted. Deep pressure over one of the scars in the right inguinal region elicited tenderness. The colon was palpable. Digital examination of the rectum and manual examination of the pelvis through the vagina revealed no abnormalities.

Examination of the urine was essentially neg-

ative. The blood at the time of examination contained 13.1 gm. of hemoglobin per 100 cc.; there were 4,690,000 erythrocytes and 8,500 leukocytes per cubic millimeter of blood. The results of proctoscopic and roentgenologic examinations of the intestine have been described. Roentgenographic examination of the chest revealed no abnormal findings. Cholecystography was attempted four days after the roentgenologic examination of the colon was completed. The functioning colon was filled with gas and the nonfunctioning colon contained enough of an opaque secretion to make satisfactory interpretation of the cholecystograms impossible. Intravenous urography was attempted the following day, but interpretation of the excretory urograms was considered to be unsatisfactory because of the large amount of gas in the functioning colon and because of the opacification of the nonfunctioning colon with the shadow-casting material it contained (Fig. 3*a* and *b*). No part of the right kidney or right ureter was made visible by the urographic contrast material but the pelvis of the left kidney was made

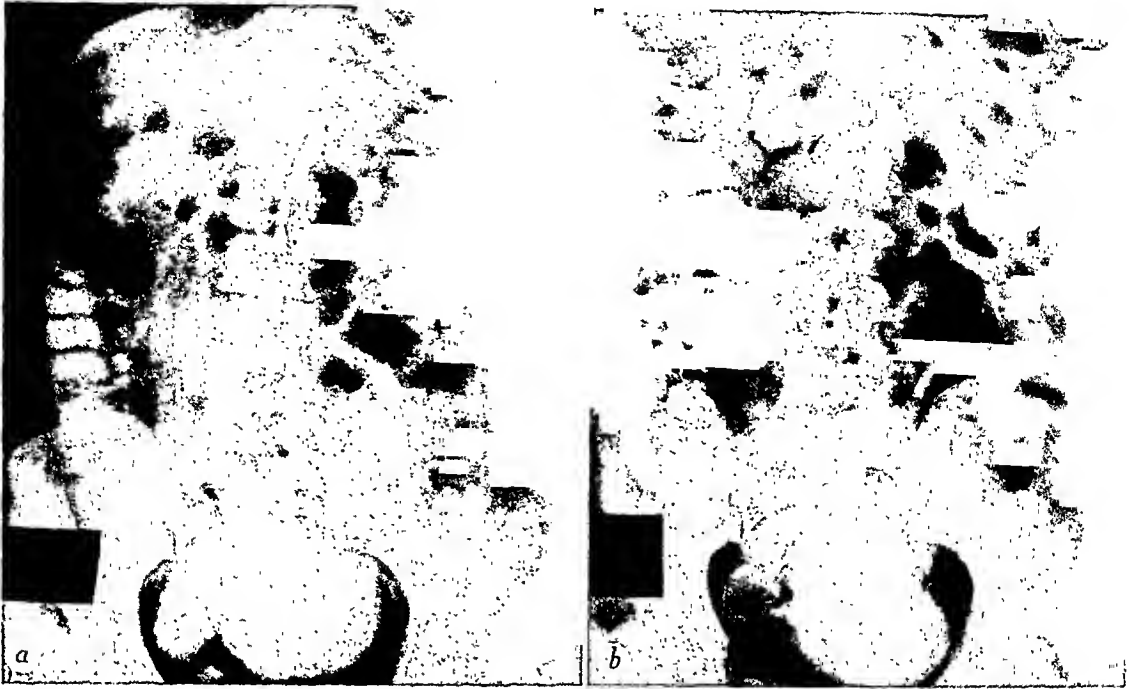


FIG. 3. Excretory urograms made five days after the roentgenologic examination of the colon: *a*, five minutes after injection of urographic medium and *b*, twenty minutes after injection of urographic medium. The normal colon is moderately distended with gas; the duplicated colon contains the same concentration of opaque material which was shown in the roentgenograms of the intestine. No shadow of kidney or ureter is seen on the right side; the pelvis of the left kidney and a portion of the left ureter may be seen at the level of the fifth lumbar vertebra. Cholecystographic examination had been done the day before; the dye-laden gallbladder is projected over the hepatic flexure of the colon on *a*.

visible as was the left ureter throughout most of its course.

Surgical exploration was advised with the idea of removing the supernumerary colon. On October 17, 1944, surgical exploration was undertaken by one of us (C. F. D.). A primary lower left rectus incision was made. Duplication of the entire colon with a common mesentery was found. The colon seemed to be about five to six times larger than normal, and the presence and the position of the longitudinal bands of the cecum and ascending colon established the fact of duplication there. The colon continued as a double organ in this manner around to the middle of the descending colon where the two colons became more distinctly separate. The vascular supply originated from the same mesentery. The most lateral portion of intestine extended down to a point just below the pelvic peritoneal fold, where, as nearly as could be determined, it ended blindly (Fig. 2*b*). This lateral segment was distended about six to eight times the size of a normal colon. A tube passed into the rectum entered the mesial portion of the duplicated bowel not the lateral segment. In the re-

gion of the first portion of the sigmoid, there was evidence of active inflammation where the lateral or blind end of the bowel had been drained previously (Fig. 1 and 2*a* at arrows). This was the site of communication of the cutaneous fistula, and in this immediate region there was also a narrow fistula, 2 or 3 mm. in diameter, running an oblique course between the normal colon and the supernumerary one. Since there was marked inflammatory reaction in this vicinity, the descending and sigmoid portions of both colons were freed from the abdominal wall, and about 8 to 10 inches (20.3 to 25.4 cm.) of each was resected after exteriorization and application of clamps. A future operation was anticipated at which time the continuity of the colon would be re-established and the spurs would be crushed in two directions in order to have the blind end of the bowel empty properly. Further exploration of the abdomen revealed the liver and gallbladder to be normal. There was no evidence of a kidney on the right side. The left kidney which was in normal position seemed by palpation to be about one and a half times normal size. Explora-

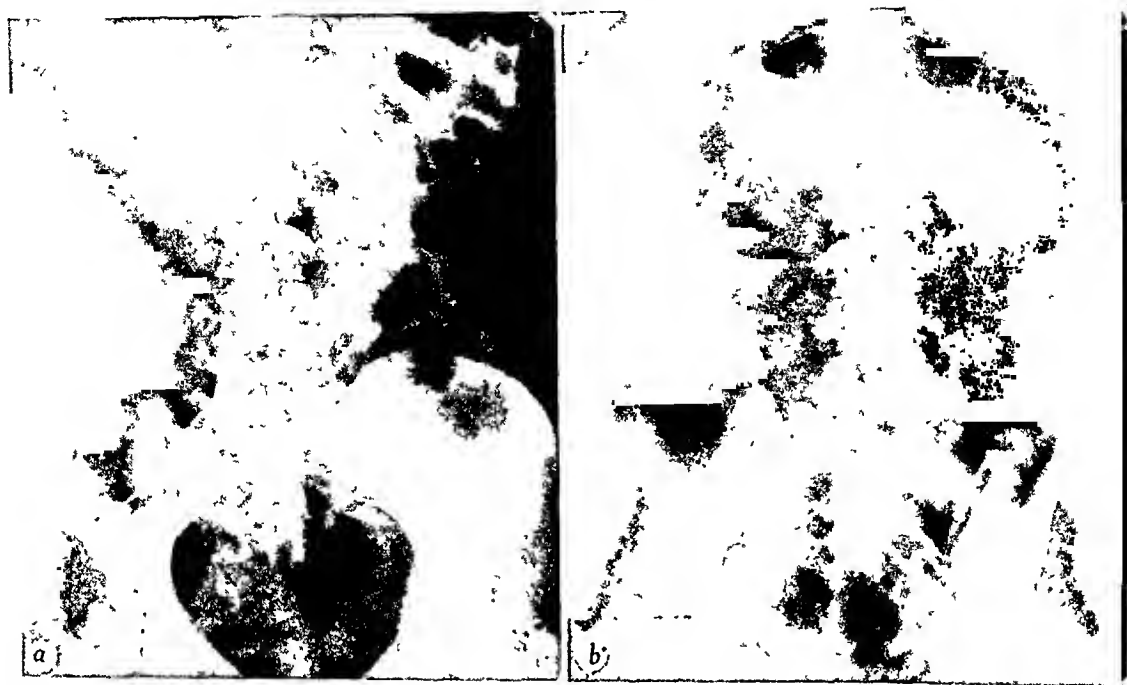


FIG. 4 *a* and *b*. Roentgenograms of the abdomen six months after operation. Other than gas-containing loops of large intestine, especially in the region of the splenic flexure, the roentgenograms reveal nothing abnormal.

tion of the pelvis revealed two infantile uteri.

MacCarty reported as follows on the specimen of 15 cm. of large intestine delivered to him for examination: "The specimen consists of two segments of large bowel, attached to each other throughout their length. One segment appears to be normal colon. The other is somewhat narrower and shows areas of superficial ulceration."

At the time of the second operation, surgical re-establishment of the continuity of the exteriorized loops of the two colons was accomplished by end-to-end anastomosis, producing what is essentially a colocolostomy in the mid-sigmoid.

The patient was seen at the Clinic again on May 15, 1945. She was still having some minor abdominal distress but seemed to be in excellent health in other respects. Roentgenographic examinations of the abdomen revealed that the remainder of the supernumerary colon no longer contained any visible opaque material (Fig. 4). With the exception of small collections of intestinal gas along the course of the large intestine, the examination of the abdomen was negative. A roentgenologic examination of the intestine with the use of contrast material was not attempted at this time.

REVIEW OF LITERATURE

We reviewed the available literature on conditions of this kind as completely as our facilities permit. Reports of duplication of the small intestine are relatively frequent. No instance was found of a duplication of the large intestine in which the supernumerary intestine had no communication with the small intestine above it nor with the outside via the rectum. This is the only example we were able to find in which duplication of the entire colon was demonstrated roentgenologically. It is also the only instance in which a correct preoperative or preneoscopic diagnosis of the condition was made.

Duhem and Monmignault, in 1936, published roentgenograms they made of a three year old child who had a duplication of the rectum and sigmoid; the patient had two anal openings, both functioning simultaneously, two vaginas and two permeable vulvae. When a colored solution was injected into one anus it came out of the other. Injection of contrast suspension

into the left anus filled a cavity which looked like a rectal ampulla; when the material was injected into the right anus it filled the cecum. Ombrédanne made a report of the same case in the same year. Ballance operated on a patient who had an imperforate anus. At the operation he discovered that there was a complete duplication of the colon extending from the rectum "nearly or quite as far as the cecum." This patient was a ten year old girl who had two rectal orifices opening into the lower and posterior vaginal wall on both sides. Injection of contrast suspension into these openings showed that there were two rectums and sigmoid colons but the rest of the colon was not outlined on the published reproduction of the roentgenograms. Gray reported an instance of triplication of the colon in an infant who was admitted to a hospital when one week old and who died nine months later. The diagnosis was made at necropsy. Grohé, in pre-roentgenologic times, reported the case of a young girl who was discovered, in a

series of laparotomies, to have a complete duplication of the large intestine complicated with many genitourinary congenital anomalies. Asai, a Japanese, also reported a case of duplication of the large intestine, the diagnosis having been made at laparotomy.

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CLUBBED FINGERS*

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THE purpose of this communication is to report certain roentgenologic findings in the arteries and arterioles, as well as to show the infra-red photographs of the superficial vessels in clubbed fingers.

MATERIAL AND METHOD

The material studied consisted of 6 cases of bilateral clubbed fingers. In 3 cases, at autopsy, the brachial arteries were injected with a suspension containing 90 gm. of barium sulfate and 180 cc. of water, after which roentgenograms were made of the hands. In 2 cases, the superficial vessels were photographed, using an infra-red filter.

CASE REPORTS

CASE 1. The patient was a woman, aged twenty-five, who died of fibroid pulmonary



FIG. 1. An arteriogram of the normal hand without clubbing of the fingers.

tuberculosis. Bilateral clubbing developed about three months prior to her death. When compared with the arteriogram of the fingers without clubbing (Fig. 1), the arterioles in this case are more numerous and prominent about the terminal phalanges, forming a comparatively heavier network about the finger tips (Fig. 2 and 3).



FIG. 2. An anteroposterior arteriogram of the hand in Case 1.



FIG. 3. An oblique arteriogram of the hand in Case 1.

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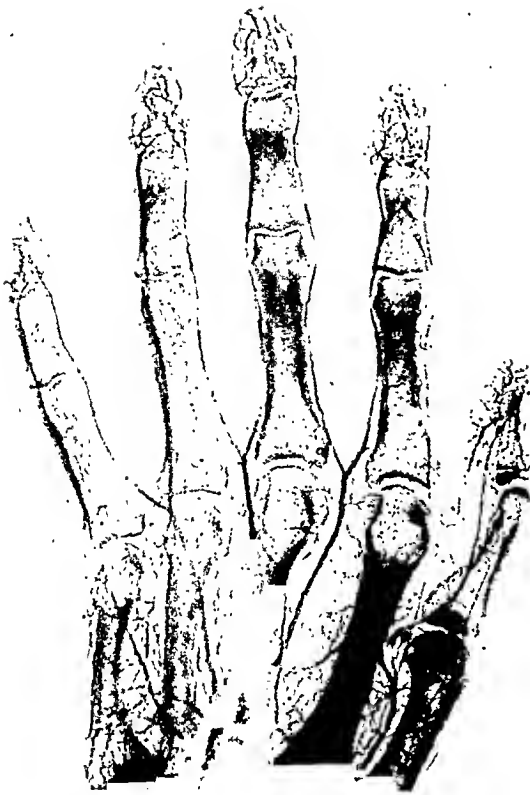


FIG. 4. An anteroposterior arteriogram of the hand in Case 11.

CASE 11. The patient was a woman, aged thirty-five, who died of fibroid pulmonary tuberculosis with a tuberculous empyema. The clubbing developed in both hands about six months prior to her death. Again the terminal arterioles appeared comparatively more numerous and dilated than in the normal control (Fig. 4 and 5).

CASE 111. The patient was an anthracite coal miner, aged forty-five. He had far advanced anthracosilicosis with superimposed ulcerocaseous pulmonary tuberculosis. The clubbing was not prominent; it developed about six months prior to his death. The multiplicity and fullness of the terminal phalangeal arterioles are again evident (Fig. 6).

CASE IV. The patient is a man, aged forty, who is now under treatment for far advanced bronchiectasis. The infra-red photograph of his hands (Fig. 7) shows that the superficial vessels are more numerous and engorged than in the control patient without clubbing (Fig. 8). There was no evidence of congestive heart failure.

CASE V. This patient is a man, aged twenty-

five, who has congenital stenosis of the pulmonary artery with a possible interventricular septal defect. Recently he developed exudative pulmonary tuberculosis. The vessels of the fingers are dilated and engorged (Fig. 9). When the arms are elevated the vessels almost completely empty and the balls of the clubbed fingers become shriveled. When the arms hang again, the vessels become engorged and the finger tips bulbous. The patient always has con-



FIG. 5. An oblique arteriogram of the hand in Case 11.

siderable cyanosis, but no signs of myocardial insufficiency.

CASE VI. This man, aged forty-two, was a patient of Dr. M. J. Sokoloff. He developed pulmonary necrosis of the left upper lobe following two attacks of what appeared to be virus pneumonia. The earliest change in the fingers was erythema of the nail beds and the thenar and hypothenar eminences of the palms. Gradually the finger tips became bulbous and the nails curved. As the necrosis of the left lung became more extensive, he developed high and irregular fever varying between 101 and 103°F. The palms perspired almost continually.

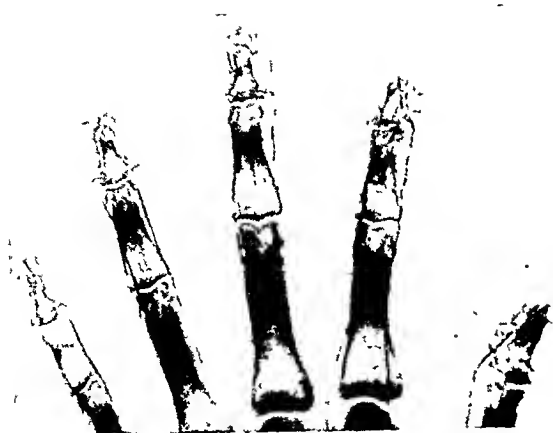


FIG. 6. An anteroposterior arteriogram of the hand in Case III.

Early in the morning, when the temperature was relatively low, urticaria appeared on the erythematous thenar and hypothenar regions of the palms associated with considerable pruritus. The urticaria recurred almost daily only on the palms until the time of lobectomy following which he died.

DISCUSSION

The roentgenologic studies in clubbed fingers thus far have dealt with the changes of the bones. The conclusions drawn have been briefly these: In the early stage there is no change of any sort.¹⁷ In the advanced cases, increased flare of the ungual process of the terminal phalanges was noted.¹² If clubbing developed during the growing period, the terminal phalanges became hypertrophied and longer than normal,¹⁸ espe-



FIG. 8. An infra-red photograph of normal hands.

cially in unilateral clubbing with venous stasis.²² In the far advanced stage, osteoporosis¹⁰ or complete resorption¹⁹ of several or all the terminal phalanges was seen. Hypertrophic osteoarthropathy of the bones of the hands with proliferation of subperiosteal new bone was a common picture. Occasionally the terminal phalanges were encapsulated with newly formed periosteal bone.¹³

In the present study on recent clubbing without osteoarthropathy, the roentgenologic studies were made with a view to demonstrate possible arterial changes in the clubbed fingers. Attempts were made to demonstrate the status of the vessels in the living by means of an opaque material (diodrast) injected into the radial arteries, but certain technical difficulties prevented obtaining satisfactory roentgenograms of the fingers. The rapidity of dilution of the

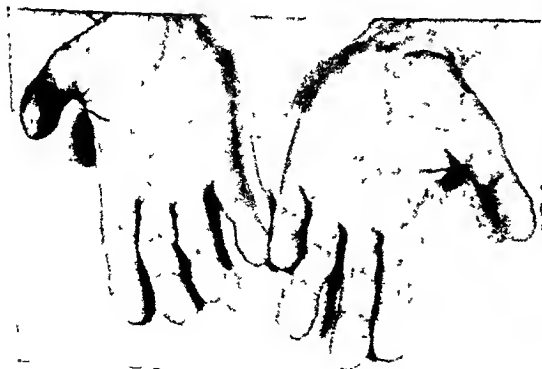


FIG. 7. An infra-red photograph of the hands in Case IV.



FIG. 9. An infra-red photograph of the hands in Case V.

opaque material and the difficulty of rapid injection made contrasting densities poor; moreover, there was difficulty in synchronizing the time of exposure with the injection. We therefore turned to the more established method, using barium.

The postmortem arteriograms showed that the arteries and arterioles were more numerous, their lumens wider, and the ungual processes were covered with a heavier network of arterioles. The infrared photographs of the clubbed fingers demonstrate greater prominence and number of the superficial vessels than normal. In the case with congenital heart disease, the increase in the soft tissues about the terminal phalanges was found to be in direct proportion to the degree of engorgement of the vessels.

The findings in these 6 cases substantiate the previous anatomic studies²⁶ which have shown dilatation and increased thickness of the vessel walls as well as a new formation of capillaries,²⁷ increase in the tissues of the finger tips, particularly in the fibrous elastic tissue of the nail beds,³¹ increase in the area of the nail and skin corresponding with the increase in volume of the underlying tissues,¹ increased thickness of the epidermal tissues,³² of the periosteum and of the ungual process of the bone itself.³⁵ Atrophy of the bone 14 had been noted in the later stages when studying the tissue sections.

Studies have been made to determine the state of blood flow in the clubbed fingers with somewhat conflicting findings. Capillary stasis with decreased blood flow and constriction of the capillaries were noted.¹¹ Dilatation and even aneurysmal loops were seen in others.²⁸ A determination of the skin temperature by means of the thermocouple showed lowered temperature in the clubbed extremity, suggesting decreased blood flow. Just the opposite findings have been encountered by others.²² These variations might have been due to different physiologic conditions present at the time of the studies, such as temperature, fear, and other emotional factors. Under regulated conditions of the environmental tempera-

ture and emotions with a relaxation of sympathetic tone, the colorimetric determinations showed increased blood flow per square centimeter in the finger tips.²² In a patient with lung abscess in which clubbing disappeared after the recovery from the disease, the blood flow was shown to return to normal.²² The antecubital venous¹⁶ and the brachial arterial²³ pressures in symmetrical clubbing were normal. The thought that the clubbing is largely hypertrophy and hyperplasia as a result of overnutrition brought about by increased peripheral blood flow seems to be a popular notion at present.

Attempts have been made to produce clubbing in experimental animals. Introduction of exudate from pulmonary abscess into the rectum,² intravenous injection of tubercle bacilli and other pyogenic organisms,⁸ paraffin injection into the lungs,⁵ ligation of the bronchi and chronic congestion³³ all failed to produce clubbing.

Hypertrophic osteoarthropathy has been produced experimentally in a dog by anastomosis of the left pulmonary artery to the left auricle. This produced a lesser circuit shunt simulating the circulatory status seen in congenital heart disease with cyanosis. The shunts were not followed by any changes of the circulation time, venous pressure, or oxygen consumption. The outstanding finding was an increase in systemic cardiac output, the blood flow through the lungs remaining comparatively normal.²⁴

Many theories have been advanced on the pathogenesis of clubbed fingers. Emaciation,¹⁵ chronic infection,²⁰ toxemia,¹⁶ capillary stasis due to back pressure from the heart and lungs,³⁴ local tissue anoxia,⁴ malfunction of the pituitary,⁹ thyroid,²¹ parathyroid glands,⁷ gonads,²¹ nerve injury,²⁹ lymph stasis,³ changes in blood volume,²⁵ increased intracranial pressure,³⁰ vitamin deficiency⁶ have been considered. Future studies will have to take into consideration the facts herewith presented. The vascular changes with an increased blood flow as shown by the present roentgenologic

study will also have to be considered as an etiologic factor.

In Case VI one wonders whether the urticaria was not in some way related to histamine-like substances liberated by the pulmonary necrosis into the blood stream. It has been shown that the pulmonary parenchyma contains a considerable concentration of histamine.

SUMMARY

Six cases of bilateral clubbed fingers were studied. In three cases the arterial systems of the hands were injected postmortem with barium sulfate suspension and roentgenograms made. In two cases the superficial vessels were visualized by photographs using an infra-red filter. In one, urticaria recurred on the palms. The common finding in these cases was increased vascularity about the clubbed fingers, particularly about the ungual processes.

The etiology of clubbed fingers is unknown. The prevailing impression seems to be that the clubbing is largely a hypertrophy and hyperplasia of the tissues about the terminal phalanges as a result of increased nutrition brought about by an increased peripheral blood flow.

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CONGENITAL DISLOCATION OF THE HIP

REPORT OF CASE

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The patient, Margaret H., was born at the Margaret Hague Maternity Hospital, Jersey City, N. J., at 6:15 A.M. on November 27, 1933, weight 2,410 grams. Because of the weight the baby was considered premature. Period of gestation was thirty-eight weeks. There was a normal spontaneous delivery. The baby was active and well nourished. Discharge from the hospital was on the eighth postpartum day. General condition was excellent. A small cutaneous depression was noted at the level of the lumbar and sacral joint, and roentgen examination was obtained of this part. That is the reason for the early roentgenograms. The report was within normal limits except for

enlarged thymus. Mother and child discharged about December 6, 1933.

On June 4, 1935, at the age of one and one-half years she was brought to the Orthopedic Clinic of the Jersey City Medical Center by her



FIG. 1. This shows the femoral head to be in place with the acetabulum.



FIG. 2. The acetabulum on each side looks the same. The right hip shows the femur farther from the pelvis than the left hip.

mother. The child had a progressive limp and lameness noticed by her parents since she commenced to walk at the age of thirteen months. Physical examination was normal except for slight shortening of the right leg. Roentgen examination revealed a definite dislocation of the right hip. Identification was made of the patient by foot prints taken at the time of birth, by records and roentgenograms, through name, hospital charts, and parents of the patient.



FIG. 3. On the right side there is a shallow acetabulum and a dislocated femoral head.

Three exposures are presented: Figure 1, lateral view of the hips and spine; Figure 2, an anteroposterior view of the pelvis and lower spine; Figure 3, a pelvis. The first two are exposures taken at time of birth and Figure 3 was

taken at the age of eighteen months. The early roentgenograms show the relation of the femoral head to the acetabulum. On the right side the femur is farther from the pelvis than the left side; also there is slight upward displacement of the femur. Figure 3 shows a classical dislocation of the hip on the right side and a partial dislocation on the left side.

Examined so close to birth this case demonstrates that there can be a dislocation before all of the mechanical factors have crept into the picture. The acetabulum is shallow and becomes more shallow with the mechanical pull of the muscles and weight bearing. The potential factor is present for dislocation and it is aggravated by the mechanical and constitutional factors. Ossification is slow on the affected side. Physical examination is helpful only in the cases with marked dislocation. The early cases might show shortening and some external rotation. After birth the hip joint is more labile in the female. This fact could account for the partial dislocation on the left side. Heredity is not always a factor. Parents with dislocation have healthy children, while most children with dislocation have healthy parents. In this case the mother and father had no hip disease.

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GIANT JUGULAR FOSSA

WITH BRIEF NOTES ON THE ANATOMICAL VARIATIONS OF THE JUGULAR FOSSA*

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IT IS common knowledge that the jugular fossa normally shows extreme developmental variations in size, shape and symmetry. The fact that the jugular bulb lies so close to the tympanic region gives it special importance in relation to otological work. This is particularly true in the occasional case with an extremely large jugular fossa, the significance of which is aptly stressed by Stiles and Fraser in Cunningham's¹ textbook as follows:

The floor of the tympanum is constituted mainly by the bone bounding the jugular fossa, which is occupied by the upper bulb of the jugular vein. When the sigmoid sinus is large and unusually far forward the bulb also is large; the fossa is consequently deeper, and arches up into the floor of the tympanic cavity, from which it may be separated merely by a thin and translucent plate of bone which occasionally shows an osseous deficiency. In cases where that condition existed the jugular bulb has been wounded in the operation of paracentesis of the tympanic membrane.

The warning that such accidents may happen is also mentioned in some otologic texts. Except for Mayer² who had the large jugular fossa well depicted in roentgenograms, there appears to be practically no mention of this condition in the roentgenological literature. The object of this report therefore is to draw the attention of roentgenologists to this relatively obscure but interesting condition.

MATERIAL STUDIED

1. *Clinical.* A patient suffering from chronic mastoiditis was seen in the Peiping Union Medical College Hospital in 1939. Details of the clinical history are, unfortunately, not available. As far as I could recollect, the patient was a young subject.

A roentgenogram of the left mastoid exposed in the Law's position on March 23, 1939, showed evidence of chronic mastoiditis with moderate sclerosis. In addition, an unusual shadow in the form of an oval, homogeneous, moderately radiolucent area (shape and size of an average grape) with a well defined thin bony wall re-



FIG. 1. Left mastoid. The giant jugular fossa is seen as an oval radiolucent area situated just below the acoustic meati.

sembling a bone cyst, was seen lying just below the shadows of the acoustic meati but with its upper border partially overlapping the inferior outline of the external acoustic meatus (Fig. 1). The long axis of this radiolucent area was almost horizontal with a slight upward inclination ventrodorsally. This shadow was taken to represent an excessively large jugular fossa. The right mastoid (Fig. 2) showed no evidence of a similar cyst-like shadow. A basal or submentovertex view of the base of the skull taken a few weeks later showed up fairly clearly the very large left jugular fossa (Fig. 3).

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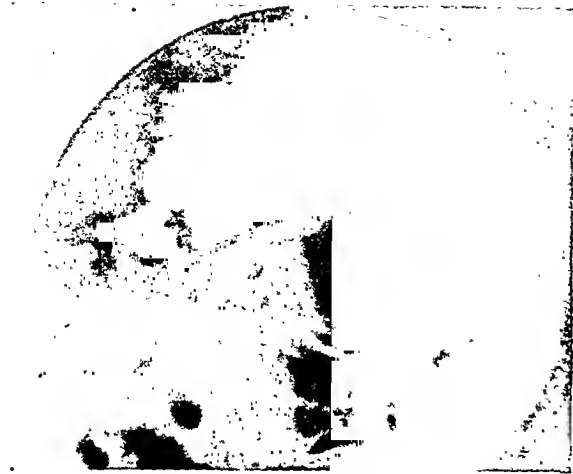


FIG. 2. Right mastoid of same case shown in Figure 1 for comparison. No similar radiolucent area seen.

A review of the mastoid roentgenograms taken in the first quarter of 1939 in the Peiping Union Medical College Hospital revealed another case with a rather large



FIG. 4. Photograph of base of skull. The right giant jugular fossa is seen lateral to the occipital condyle.

right jugular fossa, though not so pronounced as in the case described above.

2. *Anatomical.* (a) A collection of approximately 120 skulls in the Department of Anatomy of the Peiping Union Medical College was studied. A few skulls showed



FIG. 3. Basal view of skull of case shown in Figures 1 and 2. The radiolucent shadow of the left giant jugular fossa is seen lying lateral to and somewhat anterior to the transverse process of the shadow of the atlas.



FIG. 5. Roentgenogram of right mastoid of skull shown in Figure 4. The giant jugular fossa is seen as a radiolucent area below and somewhat posterior to the acoustic meati.

large jugular fossae, but there was one skull in particular that showed an unusually large right jugular fossa the foramen of which was of oval shape (Fig. 4). From a thorough roentgenological study of this specimen, it was found that only two positions, namely, the Law and submentovertex, offered good visualization for the



Fig. 6. Roentgenogram of base of skull of specimen shown in Figure 4. The right giant jugular fossa is clearly seen lateral to the occipital condyle.



Fig. 7. Roentgenogram of left mastoid of skull shown in Figure 4. No large oval radiolucent shadow is seen.

large right jugular fossa (Fig. 5 and 6). Although precise figures are not available, this extremely large right jugular fossa was probably about 2 cm. wide and 2.5-3.0 cm. deep. The left mastoid of the same skull was also roentgenographed for comparison (Fig. 7).

(b) Another investigation was conducted on a collection of 260 skulls in the museum of the School of Dentistry, National Central University. The results of this study (Table 1) shows that although the jugular fossa may be symmetrically developed in both sides (16.4 per cent), the right jugular fossa is larger than the left in the majority of cases (63.8 per cent), while the left fossa is larger than the right in only 20.8 per cent of cases. It is found

TABLE I

	a. Small Fossa (under 0.5 cm.)	b. Medium Fossa (0.5-1.0 cm.)	c. Large Fossa (over 1.0 cm.)	Total Number of Skulls and Incidence
Group 1 Jugular fossa symmetrically developed on both sides	16 skulls (40%)	24 skulls (60%)	None	40 skulls (16.4%)
Group 2 Right jugular larger than left	116 skulls (70%)	40 skulls (24%)	10 skulls (6%)	166 skulls (63.8%)
Group 3 Left jugular fossa larger than right	35 skulls (64.6%)	15 skulls (27.7%)	4 skulls (7.7%)	54 skulls (20.8%)

satisfactory to define three types of jugular fossae according to the size of their foramina, namely, (1) small (under 0.5 cm.); (2) medium (under 1.0 cm.); and (3) large (over 1.0 cm.) (see Table 1). The foramen shows considerable variation in shape, appearing in smaller fossae as fissure-like or elliptical openings, and in the larger fossae as oval or rounded apertures. The bulb or cavity of the jugular fossa is also found to vary greatly in form, from a shallow insignificant groove-like or V-shaped depression scarcely deserving the name of bulb in small fossae, to an oval, rounded or bulb-like cavity of good size in large fossae. Their interiors may be smooth or ridged, and often in the larger fossae a small rounded depression of about 2-3 mm. may be found at the topmost part or dome, the appearance of which resembles the apex of a snail's shell seen from inside.

There are 14 skulls showing large jugular fossae in this series, or an incidence of 5.4 per cent. The largest fossa measures about 1.5 cm. wide and 2.5 cm. deep. Its size, however, is mediocre when compared with the two examples described above.

Among other findings is that the transverse sinus is invariably larger in the side showing a larger jugular fossa. Also, although large jugular fossae may be found in skulls of any size, the larger fossae are usually associated with large-sized skulls.

An anomalous development is found in one right jugular fossa, namely, its foramen is completely enclosed by a ring of bone instead of being in open continuity with the foramen lacerum posterius. This abnormal foramen is rounded, and measures about 3-4 mm. in diameter.

SUMMARY

The jugular fossa normally shows considerable variation in size. Because of upward extension, the clinical significance of a large jugular fossa lies in the fact that it is apt to be punctured accidentally during paracentesis of the tympanic membrane.

An extremely large or giant jugular fossa casts an unusual grapes shaped radiolucent shadow resembling a bone cyst in roentgenograms. For roentgen demonstration of a giant jugular fossa, it is found that two views offer the best visualization, namely, the Law and the submentovertex positions.

Anatomical studies on a series of 260 skulls show that the jugular fossa is symmetrically developed in 16.4 per cent of skulls, the right jugular fossa larger than the left 63.8 per cent, and the left larger than the right 20.8 per cent. In this series, about 5.4 per cent of specimens show large jugular fossae, but there is no instance of any unusually large jugular fossa.

Based on two groups of skulls studied, the incidence of an unusually large jugular fossa appears to be about 1 in 380.

The writer is indebted to Dr. Hsu, Tien-lu of the Peiping Union Medical College and to Dr. Chen, Hua of the National Central University, for their kind permission to publish findings from their respective collection of skulls. Thanks is also due Dr. C. K. Hsieh and Dr. C. L. Hsu for other invaluable help.

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PRESENT STATUS OF ROENTGEN THERAPY OF HYPERTHYROIDISM AND RELATED ENDO- CRINE DISTURBANCES*

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IN CECIL'S well known *Textbook of Medicine*³ the chapter on the treatment of exophthalmic goiter, written by Eugene Dubois, contains the following sentences:

The operative treatment of exophthalmic goiter is the method of choice. . . . Some of the severe cases are obviously unfit for any operative procedure on account of cardiac insufficiency. Others are in the stage of rapidly increasing severity, and an operation would precipitate a crisis. Before the introduction of the use of iodine in large doses it was necessary to wait and hope that the stormy period would pass. Some of these inoperable cases did well under x-ray treatment.

A few lines below the same author writes:

Now the use of x-rays has been more or less abandoned, except in special cases where operation is refused by the patient or is inadvisable for some other reason.

Obviously these two statements contradict each other. If roentgen treatment is indicated in cases characterized by cardiac insufficiency and rapidly increasing severity of the symptoms, why has this treatment been abandoned in cases of less severity? In my opinion, the answer to this question is: Because medical thinking in every country and at all times has been prejudiced in favor of surgery, due to the lack of education in radiotherapy at the medical schools.

This prejudice is especially inappropriate in the United States since the roentgen treatment of exophthalmic goiter was first used by two American surgeons, Williams and Beck, in 1902 and 1905.

Today we are confronted with a new situation. In our last symposium, Dr. Goldzieher declared: "The surgery of

hyperthyroidism, that is, subtotal resection of the thyroid gland, is done less and less often, and internal treatment, with or without thiouracil (a compound of the sulfa group with a urea derivative) is preferable and gives excellent results." Dr. McGavack⁶ demonstrated this at the same symposium.

Thiouracil was first used in 1941 by Mackenzie and McCollum on rats affected with toxic goiter, and in 1943 Astwood administered it to patients suffering from hyperthyroidism.⁶ Characteristically enough, the most recent paper on this subject, by Bartels,¹ is entitled: "Thiouracil; Its Use in the Preoperative Management of Severe Hyperthyroidism." Here, again, we find the same prejudice in favor of surgical intervention. On the other hand, in December, 1942, Soley and Stone¹⁶ published a paper entitled: "Roentgen Ray Treatment of Hyperthyroidism" which was summarized in the *AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY* as follows:

Roentgen ray treatment of hyperthyroidism has been somewhat neglected in recent years. Therefore, the authors report a series of many cases treated in this way.

The results show that roentgen irradiation reduces thyroid tissue sufficiently to produce the same results as surgical subtotal thyroidectomy. The best patients for roentgen treatment are those with marked degree of exophthalmos.

On January 15, 1945, at a meeting of the Section of Ophthalmology of the Academy of Medicine of New York, Dr. M. N. Stow read a paper on: "The Relative Effects of Thiouracil, Iodine and Subtotal Thyroidectomy on the Exophthalmos of Hyperthyroidism." Stow stated (1) that an

* Read before the Medical Circle of New York City, January 19, 1945.

increase of the exophthalmos after subtotal thyroidectomy is a rule; even malignant exophthalmos may result; (2) that thiouracil also increases the exophthalmos, although to a minor degree, and (3) that iodine treatment for exophthalmos in hyperthyroidism is advisable. Dr. Ernest Gold, a surgeon of New York City, also did not very warmly recommend thyroidectomy in cases with marked exophthalmos, especially not in males whose goiter was not very large.

Neither Dr. Stow himself nor Dr. Barr nor Dr. Smelser, who confirmed Dr. Stow's statements, even mentioned the roentgen treatment of exophthalmic goiter. The authors only spoke against thyroidectomy and in favor of iodine treatment. From this quite recent paper, it is apparent that the roentgen treatment of exophthalmic goiter, and particularly of the pituitary, has fallen into such disuse that it is practically unknown here.

If it is true, as Dr. Goldzieher said, and I think he is right, that "the surgery of hyperthyroidism is in a state of decline," we may say that there are two methods of treating this ailment which are not in a state of decline: (1) roentgen treatment, and (2) the application of thiouracil, on which McGavack has given us such an impressive report.

In 1907¹¹ I found in collaboration with Hirschl that in cases of Graves' disease, following roentgen irradiation over the thyroid gland, the alimentary glycosuria disappeared. It then occurred to me to try roentgen irradiation of the thyroid in diabetics and I published a preliminary note on roentgen treatment in diabetics. In practice I had no success. The sugar tolerance of the diabetics did not increase. At that time, the relations between the pituitary and the thyroid were not yet known, neither the diabetogenic factor of the pituitary. So I irradiated the wrong gland. It should have been the pituitary, not the thyroid.

About the same time, I began roentgen treatment of hyperthyroidism. Since then,

I have treated altogether about 300 cases of Graves' disease in Holzkecht's Laboratory (Allgemeines Krankenhaus in Vienna), in von Noorden's Clinic and in Wenckebach's Clinic in Vienna, as well as in my private practice, including this country.

My first statistical report,¹² based upon 40 cases, reads as follows: "The tremor and resulting weakness or psychic excitement disappeared in 90% of the cases, the heart symptoms (tachycardia) in 90%, the metabolic disturbance in 60%, the exophthalmos in 40% only." This was a relatively small number, but the results were obtained by irradiation of the goiter only. I want to stress this point! The same results were obtained in all my other cases treated by roentgen irradiation. Only 10 per cent of the cases showed no improvement or discontinued the treatment.

In 1909, shortly after the publication of the favorable results of the roentgen treatment, a great discussion developed in the Vienna Medical Society.¹³ The surgeons were opposed to roentgen treatment of Basedow's disease; and, in particular, von Eiselsberg warned against the formation of adhesions which might prove a great obstacle to surgery should a resection of the goiter later become necessary. But in 1924 von Eiselsberg himself declared that these feared adhesions were negligible. In the same debate, not only surgeons and radiologists but also neurologists, physiotherapists, climatologists and general practitioners participated, expressing their views on the treatment and etiology of exophthalmic goiter. Winternitz, a prominent physiotherapist, provoked the audience to laughter when he described a peculiar case, dating from an early period when nothing was known about the connection between the pituitary, the sex hormones and the thyroid gland.

I collected my material carefully and again published my experiences in 1921¹⁴ and 1928.¹⁵ In 1925, Dr. Hans Pollitzer, an assistant at Ortner's Clinic (Allgemeines Krankenhaus, Vienna), demonstrated what he termed cases of Basedow's disease of

hypophyseal origin. These cases were characterized by the absence of the thyroid gland, pronounced tremor and high grade increase of the metabolic rate. Iodine treatment had no effect. Pollitzer's important contribution was also based on a purely clinical observation. In 1926, Borak² for the first time published good results of roentgen treatment of the hypophysis, especially in post-climacteric women. This was a great step forward in roentgen therapy. However, this observation was not given a great deal of attention in America, although the good influence of roentgen irradiation of the pituitary in acromegaly, due to the decrease of excessive growth hormone of the pituitary's anterior lobe (first described by B  cl  re in 1909), was reviewed by Percival Bailey from Cushing's Clinic in 1925.

After 1932, when Loeb discovered a thyrotropic hormone in the hypophysis, the whole subject was put on a clear experimental basis. Still more interesting is the fact that exophthalmos can be induced more readily in a thyroidectomized animal than in an intact animal by injection of a hormone of the anterior lobe of the pituitary gland, which usually was identified with the thyrotropic hormone. In this respect Marine and Rosen's⁷ (1933) and Smelser's experiments in 1937 on guinea pigs were decisive. One may term this hormone sympathico- or better adreno-tropic (Collip) or exophthalmogenic. Thyrotropic would be the wrong term because this kind of exophthalmos has nothing in common with the thyroid or thyroxin. Incidentally, Raab and Hutton irradiate the adrenal region in essential hypertension. According to Mayo, the blood pressure in toxic adenoma is always increased and exophthalmos is rare, whereas in "true" Basedow's disease the blood pressure is not increased but exophthalmos is always present. It would be appropriate in every case of hyperthyroidism to irradiate the pituitary also, and to irradiate, as I have already said, the pituitary in diabetes on account of the increased diabetogenic

factor. It is still unknown from which cells of the pituitary's anterior lobe this exophthalmogenic hormone is secreted, but its close relationship with the gonadotropic hormone, perhaps prolactin B, appears probable.

One of my latest observations, made here in New York, was of a young woman, about twenty-eight, who suffered from Graves' disease and amenorrhea. Roentgen treatment of the thyroid improved her condition considerably, as regards the tremor, metabolic rate and tachycardia, but the exophthalmos did not show adequate improvement until the hypophysis was irradiated. Simultaneously with the disappearance of the exophthalmos regular menstruation was resumed.

Returning briefly to the history of roentgen treatment of hyperthyroidism, it is noteworthy that Portmann,¹⁰ in "The Science of Radiology," writes:

The beginning of roentgen therapy for exophthalmic goiter should be credited to Williams (1902). Carl Beck discussed it but advocated operation, leaving the wound open and applying irradiation postoperatively. It was not until several years later that favorable reports on the treatment of goiter began to appear in the literature in numbers. In 1904 Charles H. Mayo stated that he had observed the "sclerosing effect," which roentgen therapy produced in cervical lymph adenitis and concluded that the glandular activity of the thyroid might be reduced, and therefore had treated ten cases, making it a rule "in severe cases of exophthalmic goiter to treat by roentgen rays preoperatively for from two to six weeks." In 1906 Pfahler and Thrush⁸ made a report of thirty-one cases collected from the literature and their own experience.

As mentioned before, my own experiences with this treatment commenced in 1908 and were neither pre- nor post-operative, but purely roentgen therapeutic applications.

Pfahler and Vastine,⁹ reviewed more than 400 cases, of which 88 per cent improved. Soiland reported on 3,000 cases with about the same percentage of improvement.

A highly accurate contribution to our subject was published in 1929, by Solomon,¹⁷ of Paris. He reviewed about 200 cases treated by roentgen radiation, stressed that operations have an average mortality of 7 per cent, and found that after roentgen treatment of his own 100 cases of Graves' disease, 70 per cent were cured, 27 per cent improved, and 3 per cent refractory. Solo-

tary. This fact, together with my own observations, must lead to the conclusion that there are two kinds to exophthalmos, one pituitary in origin, and one thyroid in origin.

My own technique of application of the roentgen rays is based on the principle that Graves' hyperthyroid goiter should never be irradiated in one massive dose. The



FIG. 1. *A*, recurrent hyperthyroidism after operation. Exophthalmos increased. *B*, exophthalmos reduced after roentgen treatment of the thyroid. (From Solomon.¹⁷)

mon also pointed out that 25 per cent of cases of Graves' disease recur after operation.

In these recurrent cases also roentgen therapy achieves excellent results. Figure 1 concerns one such case. The exophthalmos was moderate after thyroidectomy, but the eyelids were very much more widened than before the operation and gave the patient the well known frightened look. Directly contradicting Dubois, Solomon declares that roentgen treatment is the method of choice. There is no mortality unless the heart has been severely damaged previously. It should be noted that Solomon irradiated the thyroid only, not the pitui-

patient should always first be studied roentgenologically to ascertain whether a retrosternal goiter is present. Obviously a thoracic (retrosternal) goiter should also be irradiated. The average total dose for one series (three applications in one week) to the thyroid gland is 450 r, one from above and one from each side. The single dose is about 150 r. As a matter of routine, I always protect the larynx with a piece of lead rubber. I use about 160 kv. and a filter of 0.5 mm. Cu plus 1 mm. of aluminum. If this method of divided doses is used, the so-called early deep reaction, which may lead to a deep hyperemia and to initial increase in the thyroxin resorption,

never occurs. The first criterion of the effectiveness of the irradiation is the lowering of the basal metabolic rate. The increase in weight of the patient is usually apparent three weeks after the first series. If there is no considerable improvement after the first series, a second one and even a third series should be applied. In every case with marked exophthalmos the hypophysis should also be irradiated from the frontal and from both temporal sides, each dose being 200 r at 160 kv. with 0.5 mm. Cu filter.

When this method of small fractionated doses is used, the danger of myxedema described by Richardson in 4 irradiated cases of Graves' disease is avoided. Rother correctly points out that myxedema occurred also in cases of Graves' disease which were absolutely untreated. At any rate, I have put this risk in my material as negligible.

Comparing the thiouracil treatment with the roentgen treatment, we can see that both methods have nearly the same curative effect. The underlying biological process is obviously the same in both methods: a depression of the glandular function. No instance of a stimulating effect of roentgen rays has ever been proved. Roentgen rays suppress hyperactivity of cells in growth or function. Incidentally, it is interesting to note that if the whole body is subject to irradiation by roentgen rays or if any radioactive substance is injected, agranulocytosis may also result. But this danger does not exist with roentgen treatment which is localized to the thyroid or hypophysis. On the other hand, the thiouracil treatment does not require any apparatus. The danger of agranulocytic angina and other serious conditions can be avoided by lowering the maintenance dose. The so-called social indication exists in both methods.

At the Congress of Clinical Endocrinology (September, 1944) Grollman and Clifford suggested a combination of thiouracil therapy and roentgen irradiation as a substitute for the usual administration

of iodine followed by thyroidectomy. They give 0.1 gm. of thiouracil six times a day for five days only. Considering that roentgen irradiation usually does not result in improvement before the lapse of some weeks, whereas thiouracil may cause the basal metabolic rate to begin to improve within only five days, thiouracil treatment followed by roentgen irradiation seems reasonably indicated.

In an article by Gargill and Lesses⁵ published April 7, 1945, in which the danger of thiouracil in thyrotoxicosis was discussed, roentgen treatment is not even mentioned. I think it noteworthy that as late as July, 1945, in an article by Fishberg and Vorzimer⁴ roentgen therapy of the thyroid and pituitary is not mentioned. It appears that at present there is only the choice between subtotal thyroidectomy, iodine therapy and thiouracil medication.

As roentgen rays suppress chiefly *hyperactivity* of cell growth and cell function, a normal thyroid or parathyroid is not affected by roentgen irradiation, but since a hyperactive and hypertrophic parathyroid probably will be affected by thiouracil or roentgen treatment, the disease termed osteitis fibrosa cystica appears to be a proper indication for an attempt to use thiouracil also. The drug thiouracil will perhaps act favorably in myelogenous leukemia, in generalized or non-generalized roentgen sensitive cancer or sarcoma. Radium and thorium X salts, which by their radioactivity are related to roentgen rays, are stored in the bone marrow and thiouracil is also stored there, although not, like radium salts, permanently, a fact which makes the injection of those radioactive salts so dangerous.

At the above mentioned Congress, Astwood stated that if thiouracil medication is stopped too early the metabolic rate rises again within five to forty-five days. However, when treatment with thiouracil was maintained for a period of from six to nine months, a continued remission occurred. But since a prolonged administration of the drug may result in agranulocyto-

sis and other toxic reactions, the combined thiouracil-roentgen treatment should, at present, be regarded as the method of choice. Since roentgen treatment gives permanent results it should never be omitted.

CONCLUSIONS

(1) The roentgen treatment of hyperthyroidism is a well proved method, giving at least the same good results as surgery and iodine treatment without any risk to the patient.

(2) The roentgen treatment of the pituitary gland should not be omitted, especially in cases with pronounced exophthalmos.

(3) Although thiouracil treatment is at present regarded as the method of choice, only competing with subtotal thyroidectomy or iodine treatment, the apparently forgotten roentgen treatment should be reinstated to its former important place.

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Editorial Board: A. C. Christie, E. H. Skinner, Lauriston S. Taylor.

Advisory Board for Pathology: Eugene L. Opie.

Forty-seventh Annual Meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Sept. 17-20, 1946.

AMERICAN RADIUM SOCIETY

President: William E. Costolow, Los Angeles, Calif.; *President-Elect:* Charles L. Martin, Dallas, Texas; *1st Vice-President:* Frank E. Adair, New York, N. Y.; *2nd Vice-President:* Eugene P. Pendergrass, Philadelphia, Pa.; *Secretary:* A. N. Arneson, 4952 Maryland Ave., St. Louis, Mo. (*Acting Secretary,* E. H. Skinner, 1532 Professional Bldg., Kansas City, Mo.); *Treasurer:* Leland R. Cowan, 606 Medical Arts Bldg., Salt Lake City, Utah.

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Representatives on American Board of Radiology: Douglas Quick, New York, N. Y., B. P. Widmann, Philadelphia, Pa., F. W. O'Brien, Boston, Mass.

Twenty-eighth Annual Meeting: 1946, to be announced.

EDITORIAL

PNEUMOTHORAX IN YOUNG ADULT MALES

THE occurrence of spontaneous pneumothorax is not so infrequent as has been thought. Such reports as have appeared in the literature have dealt with small groups of cases or with those which have presented unusual features or complications. Most of the reports in which large numbers of cases are given have come from clinics or sanatoria dealing with tuberculous patients. Therefore it is of considerable interest to have a report on a large group of young adult males in which spontaneous pneumothorax occurred.

Such a study has recently been published by Lieutenant Colonel John E. Leach.¹ His report is based on 126 patients with 129 episodes of spontaneous pneumothorax observed among the military personnel in an Army Air Forces Training Command. Since all the military personnel had a roentgenogram of the chest made prior to entrance into the service and since many have roentgenograms made on entering active duty, the report dealing with such a group is of extreme interest and importance.

In the 126 male patients with spontaneous pneumothorax, one patient had one recurrence and one patient had two recurrences during the period covered by the survey. The ages of the men ranged from eighteen to forty-one years and averaged 24.8 years. It is of interest to note that there were no immediate fatalities in the group.

It has been taught and believed that the onset of spontaneous pneumothorax is usually sudden and is often associated with pronounced symptoms of dyspnea, pain in the chest, pallor and evidences of cardiovascular embarrassment. Contrary to this

general belief and observation, in the patients reported in Leach's study the onset of the pneumothorax was gradual in an appreciable portion. In another appreciable portion the initial symptoms were either non-existent or quite mild in character, and the difference between those exhibiting no symptoms or only mild ones (63.5 per cent) and those exhibiting moderate and severe symptoms (36.5 per cent) is statistically significant. Leach suggests the possibility that the generally high state of physical fitness of the men in the Air Forces contributed to the mildness of the symptoms.

In the analysis of his cases he found no association between the severity of the reported symptoms at the onset of the attack and the degree of pulmonary collapse. In 76 of the total cases there was nothing in the past medical history that had any reasonable association with the onset of spontaneous pneumothorax. Eighteen of the patients had infections of the upper respiratory tract, many of which were mild. Although thirteen of the patients had an infection of the upper respiratory tract associated with cough, it is significant that in only one instance did the pneumothorax occur during a period of coughing.

It is of extreme significance that in the total 129 cases reported in Colonel Leach's survey, not one occurred during aerial flight. It is of considerable interest that in a higher percentage of the cases reported, the onset of pneumothorax was associated with a minimum of physical activity and in only a significantly lower percentage of cases was the onset associated with extreme physical activity.

This finding suggested to Leach two possible explanations: First, the amount of physical activity has little to do with the

¹ Leach, J. E. Pneumothorax in young adult males. *Arch. Int. Med.*, 1945, 76, 264-268.

onset of the average case of spontaneous pneumothorax, or second, the cause of the pneumothorax occurring at rest is quite different from the cause of that occurring during exercise. There was apparently in this group of cases no association between the amount of physical activity and either the symptoms or the degree of collapse of the lung at the onset.

In the group of cases reported, the valvular type of pneumothorax was an unusual occurrence.

It has been noted before, by Ornstein and Lercher,² that the more frequent occurrence of spontaneous pneumothorax is on the right side and in the survey by Leach this also held true; 59.8 per cent of the occurrences were on the right side. While this is significant, it was not apparent from this study why spontaneous pneumothorax occurs more frequently on the right side.

The estimation of the percentage of collapse in pneumothorax is difficult, as Leach says, because of the differences of methods among roentgenologists in estimating the percentage and also variations in the technique of making roentgenograms. However, in this series of cases, the patients had degrees of pulmonary collapse estimated at below 33 per cent.

The cause of the spontaneous pneumothorax was not determined for a great majority of the patients. Leach emphasizes the fact that subpleural emphysematous blebs or visceroparietal pleural adhesions could not be demonstrated on the roentgenograms but that these might have been present without their having been demonstrated.

Complications during the course of the pneumothorax were infrequent. The average length of hospitalization of the patients was 39.9 days, and 31.1 days was the av-

erage number required for the air to be reabsorbed.

It is of significance that of the 126 persons reported in this survey, 93 were retained in military service. It is also of significance that of the 41 patients who were flying personnel, the trained personnel and the student officers were either restored to flying directly after hospitalization or were suspended from flying up to twelve months and then restored, whereas the aviation cadets and aviation students, for the most part, were physically disqualified for further flying duty.

In this group, there were seven patients who gave a positive history of previous pneumothorax. These seven patients had a total of eleven previous episodes of pneumothorax and it is of interest to note that five of the seven patients had recurrences on the right side; it is also noteworthy that these recurrences were not associated with unusual physical activity.

It is extremely important that so large a group of healthy young adult males exhibiting spontaneous pneumothorax has been collected and analyzed. Contrary to what has been generally believed, the vast majority of these, namely in 85 out of 100 cases, the onset of the attack occurred when the patient was at rest or during only mild physical activity. The frequency of the occurrence of spontaneous pneumothorax on the right side is still not explained. Certain other facts of importance are gleaned from this report, namely that, on the average, the air can be expected to be absorbed in about twenty days in those patients who exhibit less than 50 per cent pulmonary collapse.

It is of importance to note that from an analysis of these cases Leach arrived at the conclusion that there is no demonstrable relation between flying and spontaneous pneumothorax.

² Ornstein, G. G., and Lercher, L. Spontaneous pneumothorax in apparently healthy individuals. *Quart. Bull. Sea View Hosp.*, 1942, 7, 149-187.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY

Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Sept. 17-20, 1946.

AMERICAN COLLEGE OF RADIOLOGY

Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION

Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio. Annual meeting: San Francisco, Calif., July 1-5, 1946.

ARKANSAS RADIOLOGICAL SOCIETY

Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

RADIOLOGICAL SOCIETY OF NORTH AMERICA

Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1946, to be announced.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY

Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION

Secretary, Dr. Gordon G. King, 3700 California St., San Francisco 18, Calif.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY

Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY

Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL ASSOCIATION

Secretary, Dr. Roy W. Johnson, 1407 S. Hope St., Los Angeles, Calif. Meets on second Wednesday of each month at the County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION

Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY

Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N. Y. Meets monthly on fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY

Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

CHICAGO ROENTGEN SOCIETY

Secretary, Dr. F. H. Squire, 1754 W. Congress St., Chicago 12, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY

Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY

Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

DALLAS-FORT WORTH ROENTGEN STUDY CLUB

Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meetings held in Dallas on odd months and in Fort Worth on even months, on third Monday, at 7:30 P.M.

DENVER RADIOLOGICAL CLUB

Secretary, Dr. A. Page Jackson, Jr., 1612 Tremont Place, Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY

Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA RADIOLOGICAL SOCIETY

Secretary, Dr. J. F. Pitman, Blanch Hotel Annex, Lake City, Fla. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY

Secretary, Dr. James J. Clark, 478 Peachtree St., Atlanta, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

RADIOLOGICAL SOCIETY OF KANSAS CITY

Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

ILLINOIS RADIOLOGICAL SOCIETY

Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY

Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meets annually second Sunday in May.

IOWA X-RAY CLUB

Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

KENTUCKY RADIOLOGICAL SOCIETY

Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

LONG ISLAND RADIOLOGICAL SOCIETY

Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

LOUISIANA RADIOLOGICAL SOCIETY

Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS

Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

MILWAUKEE ROENTGEN RAY SOCIETY

Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY

Secretary, Dr. Annette T. Stenstrom, 1218 Medical Arts Bldg., Minneapolis, Minn. One meeting a year at time of Minnesota State Medical Association.

NEBRASKA RADIOLOGICAL SOCIETY

Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY

Secretary, Dr. Richard C. Batt, Berlin, N. H. Four meetings a year.

RADIOLOGICAL SOCIETY OF NEW JERSEY

Secretary, Dr. H. R. Brindle, 501 Grand Ave., Asbury Pk. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

NEW YORK ROENTGEN SOCIETY

Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY

Secretary, Dr. Major Fleming, Rocky Mount, N. C. An-

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

- nual meeting, Carolina Hotel, Pinehurst, N. C., May 1, 1946.
- NORTH DAKOTA RADIOLOGICAL SOCIETY**
Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.
- CENTRAL NEW YORK ROENTGEN RAY SOCIETY**
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.
- OHIO RADIOLOGICAL SOCIETY**
Secretary, Dr. Henry Snow, 1061 Reibold Bldg., Dayton, Ohio. Meets during annual meeting of Ohio State Medical Association.
- PACIFIC ROENTGEN SOCIETY**
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.
- PENNSYLVANIA RADIOLOGICAL SOCIETY**
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport. Annual meeting, Berkshire Hotel, Reading, Pa., May 17-18, 1946.
- PHILADELPHIA ROENTGEN RAY SOCIETY**
Secretary, Dr. C. L. Stewart, Jefferson Hospital, Meetings first Thursday of each month, October to May, at 8:00 P.M., in Thomson Hall, College of Physicians, 21 S. 22d St.
- PITTSBURGH ROENTGEN SOCIETY**
Secretary, Dr. L. M. J. Freedman, 4800 Friendship Ave. Meets 6:30 P.M. at The Ruskin on second Wednesday, each month, October to May inclusive.
- ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.**
Secretary, Dr. Murray P. George, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.
- ROCKY MOUNTAIN RADIOLOGICAL SOCIETY**
Secretary, Dr. A. M. Popma, 220 N. First St., Boise, Idaho.
- ST. LOUIS SOCIETY OF RADIOLOGISTS**
Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.
- SAN DIEGO ROENTGEN SOCIETY**
Secretary, Dr. Henry L. Jaffe, Naval Hospital, Balboa Park, San Diego, Calif. Meets monthly on first Wednesday at dinner.
- SAN FRANCISCO RADIOLOGICAL SOCIETY**
Secretary, Dr. Joseph Levitin, 516 Sutter St., San Francisco 2, Calif. Meets monthly on the third Thursday at 7:45 P.M., first six months of the year at Lane Hall, Stanford University Hospital, and second six months at Toland Hall, University of California Hospital.
- SHREVEPORT RADIOLOGICAL CLUB**
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.
- SOUTH CAROLINA X-RAY SOCIETY**
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.
- TENNESSEE RADIOLOGICAL SOCIETY**
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.
- TEXAS RADIOLOGICAL SOCIETY**
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting, Dallas, Texas, Monday, January 14, 1946.
- UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING**
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.
- UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE**
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00-5:00 P.M., Room 301, Service Memorial Institute.
- VIRGINIA RADIOLOGICAL SOCIETY**
Secretary, Dr. E. L. Flanagan, 116 E. Franklin St., Richmond, Va. Meets annually in October.
- WASHINGTON STATE RADIOLOGICAL SOCIETY**
Secretary, Dr. Thomas Carlile, 1115 Terry St., Seattle. Meets fourth Monday each month, October through May, College Club, Seattle.
- X-RAY STUDY CLUB OF SAN FRANCISCO**
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly, third Thursday evening.

CUBA

- SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA**
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

BRITISH EMPIRE

- BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY**
Medical Members' meeting held monthly on third Friday at 2:30 P.M. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.
- SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)**
Meets on the third Friday of each month at 4:45 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.
- FACULTY OF RADIOLOGISTS**
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.
- SECTION OF RADIOLOGY AND MEDICAL ELECTRICITY, AUSTRALASIAN MEDICAL CONGRESS**
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.
- RADIOLOGICAL SECTION OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION**
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.
- CANADIAN ASSOCIATION OF RADIOLOGISTS**
Secretary, Dr. J. W. McKay, 1620 Cedar Ave., Montreal, P. Q.
- SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES**
Secretary, Dr. Origène Dufresne, 4120 Ontario St., East Montreal, P. Q.
- SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION**
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.
- RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MEDICAL ASSOCIATION**
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

SOUTH AMERICA

- SOCIEDAD ARGENTINA DE RADIOLOGIA**
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.
- SOCIEDAD PERUANA DE RADIOLOGIA**
Secretary, Dr. Victor Giannoni, Apartado, 2306, Lima, Peru. Meetings held monthly except during January, February and March, at the Asociación Médica Peruana "Daniel A. Carrión, Villalta, 218, Lima.

CONTINENTAL EUROPE

- SOCIEDAD ESPAÑOLA DE RADIOLOGIA Y ELECTROLOGIA**
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.
- SOCIÉTÉ SUISSE DE RADIOLOGIE (SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT)**
Secretary for French language, Dr. Babaianz, Geneva. *Secretary* for German language, Dr. Max Hopf, Effingerstrasse 49, Bern. Meets annually in different cities.
- SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE**
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. 1., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.
- ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD: USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.**
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.
- LENINGRAD ROENTGEN RAY SOCIETY**
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.
- MOSCOW ROENTGEN RAY SOCIETY**
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.
- SCANDINAVIAN ROENTGEN SOCIETIES**
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

DEVICE FOR PREPARATION OF EYES FOR ROENTGENOSCOPY

To the Editor:

The ordinary so-called roentgenoscopy goggles have been used many years for preparation of the eyes for roentgenoscopy and protection against white light between cases examined roentgenoscopically. These goggles are cumbersome, uncomfortable and conspicuous. After experimenting for some months with a filter material covering only the area of my glasses, I have found that white light reaching the retina around the edge of the glasses does not affect greatly the sensitivity of the eye to the roentgenoscopic image. I submitted this idea to others, who also conducted experiments to determine if there were any considerable loss in efficiency in using a proper filter covering only the area of one's eye glasses. They reported that their findings were essentially the same as mine. Therefore, with the cooperation of the Picker X-ray Company, I had some clip-on frames with plastic filter made. I have used these lenses for several weeks and am pleased by the fact that I can drive my car to the office and be prepared for roentgenoscopic work in nearly as short a time as I could by wearing the old style mask type of goggles. Inasmuch as these clip-on filters are light, inconspicuous, and can be carried in the pocket, I believe that they are a great improvement over the previous devices available. For those who do not wear spectacles, plastic lenses can be mounted in ordinary spectacle frames.

FRANK E. WHEATLEY, M.D.

129 West Elm St.,
Brockton, Massachusetts

NEED FOR RADIOLOGICAL LITERATURE IN BELGIUM

To the Editor:

We beg to inform you that our association created some years ago a Library especially devoted to the problems of cancer and which is at the disposal of the four

Schools of Medicine of Belgium. As we were much deprived of any American medical or radiological literature during the war, we would be very glad if the members of your Society would send to the Library reprints or any published works dealing with the cancer problem. Please accept our best thanks in anticipation.

Ligue nationale belge contre le cancer

A. VANDENITTE, Librarian

rue des Deux Eglises, 21

Bruxelles, Belgium

NORTH CAROLINA RADIOLOGICAL SOCIETY

The annual meeting of the North Carolina Radiological Society will be held at the Carolina Hotel, Pinehurst, North Carolina on Wednesday, May 1, 1946. The following program will be presented:

9:30 A.M. BUSINESS SESSION—Report of committees and election of officers

11:00 A.M. FILM READING SESSION—"Stump the Experts"

Fred Jenner Hodges, M.D., Professor of Roentgenology,
University of Michigan, Ann Arbor, Michigan

EXPERTS: Robert J. Reeves, M.D., Professor of Radiology,
Duke University, Durham, N.C.

James P. Rousseau, M.D., Professor of Radiology,
Bowman-Gray Medical School, Winston-Salem, N.C.

CASE PRESENTATIONS BY:
Allan Tuggle, M.D., Charlotte, N.C.

Graham Barefoot, M.D., Wilmington, N.C.

O. D. Baxter, M.D., Charlotte, N.C.

G. W. Murphy, M.D., Asheville, N.C.

B. E. Rhudy, M.D., Greensboro, N.C.

12:00 Noon to 2:00 P.M. LUNCH—Carolina Hotel

2:00 P.M. CONTINUATION OF FILM READING
SESSION:

EXPERTS: The Same

CASE PRESENTATIONS BY:

C. L. Gray, M.D., High Point,
N.C.

J. E. Hemphill, M.D., Charlotte,
N.C.

L. W. Oehlbeck, M.D., Morgan-
ton, N.C.

W. W. Vaughan, M.D., Durham,
N.C.

3:00-4:00 P.M. "IT PAYS TO CATALOGUE
X-RAY EXPERIENCES"

Fred Jenner Hodges, Professor
of Roentgenology,
University of Michigan, Ann
Arbor, Michigan

4:30 P.M. SOCIAL ACTIVITIES

DAVID ANDERSON-BERRY PRIZE

A David Anderson-Berry Silver-gilt Medal, together with a sum of money amounting to about £100, will be awarded in 1947 by the Royal Society of Edinburgh to the person, who, in the opinion of the Council, has recently produced the best work on the therapeutic effect of roentgen rays on human diseases.

Applications for this prize are invited. They may be based on both published and unpublished work and should be accompanied by copies of relevant papers.

Applications must be in the hands of the General Secretary, Royal Society of Edinburgh, 22 George Street, Edinburgh 2, by December 1, 1946.

NEW OFFICERS

The following are the recently elected officers of the American Roentgen Ray Society for the year 1945-1946: *President*: Dr. Ross Golden, New York, N. Y.; *President-Elect*: Dr. Raymond C. Beeler, Indianapolis, Ind.; *First Vice-President*: Dr. Francis F. Borzell, Philadelphia, Pa.; *Second Vice-President*: Dr. Ellis R. Bader, Cincinnati, Ohio; *Secretary*: Dr. H. Dabney Kerr (re-elected), Iowa City, Iowa; *Treasurer*: Dr. J. Bennett Edwards (re-elected), Leonia, N. J.

AMERICAN BOARD OF RADIOLOGY

The American Board of Radiology will conduct examinations at the Palmer House, Chicago, Illinois, on November 27 to December 1, 1946. This will be the only examination held during 1946. All those wishing to appear before the Board at this time *must* have their application on file by September 1, 1946.

B. R. KIRKLIN, Secretary
American Board of Radiology
Mayo Clinic, Rochester, Minn.



DEPARTMENT OF TECHNIQUE

Department Editor: ROBERT B. TAFT, M.D., B.S., M.A., 103 Rutledge Ave.
Charleston, S. C.

ELEMENTS OF ROENTGEN TECHNIQUE

THE UNIVERSAL DISTINCTOR OF HOLZKNECHT-INGBER IN THE EXAMINATION OF THE GASTROINTESTINAL TRACT*†

By EDMUNDO INGBER, M.D.
CORDOBA, ARGENTINA

IN THE early days of roentgen diagnosis of the gastrointestinal tract, Holzknecht devised two instruments, namely, the *spoon-shaped distinctor* for localization and controlled compression in a space 5 by 8 cm., and the *button distinctor* for the controlled compression and exact localization within an area of 1 to 2 cm. in diameter.

These are two wooden instruments carefully worked out by Holzknecht and adapted to all the demands of roentgen palpation which are encountered in its practical application every day; they have been substituted advantageously for the old method of palpation with the hand protected by the lead glove, which to be sure

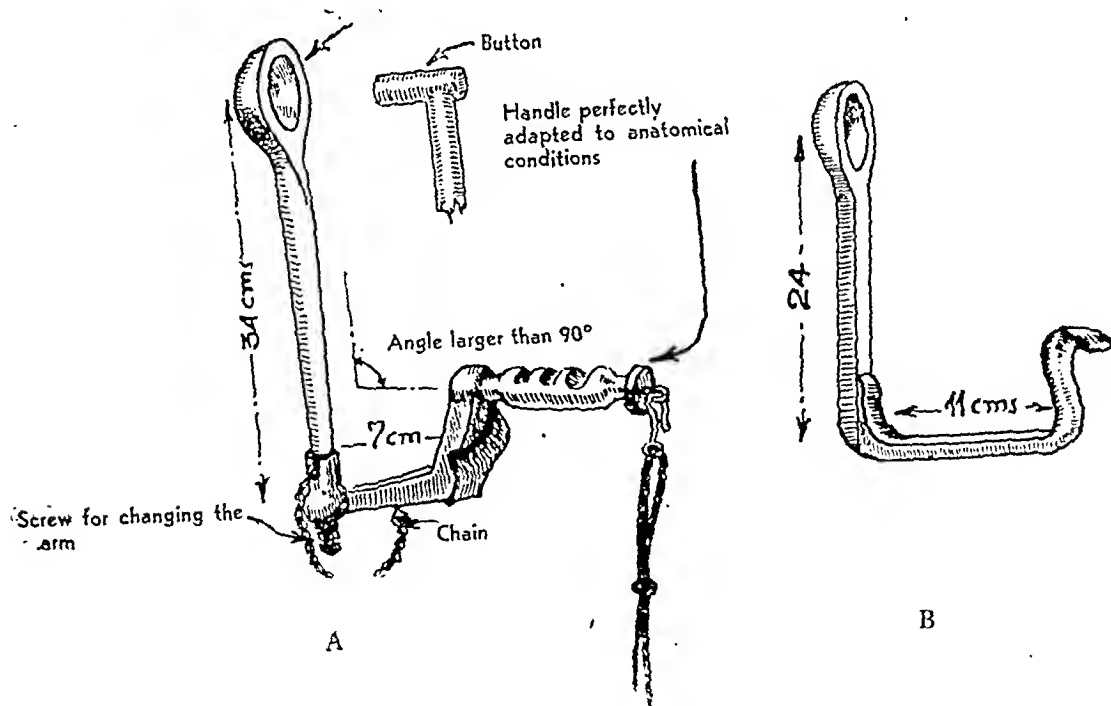


FIG. 1. A, universal spoon and button distinctor of Holzknacht-Ingber which fulfills all the requirements of roentgen palpation. B, imitation form of spoon distinctor derived from Holzknecht's which is of no practical use.

* Presented at the Discussions on Digestive Pathology, Italian Hospital of Santa Fe, August, 1942.

† Translated from the Spanish by Audrey G. Morgan, M.D., Medford, Oregon.

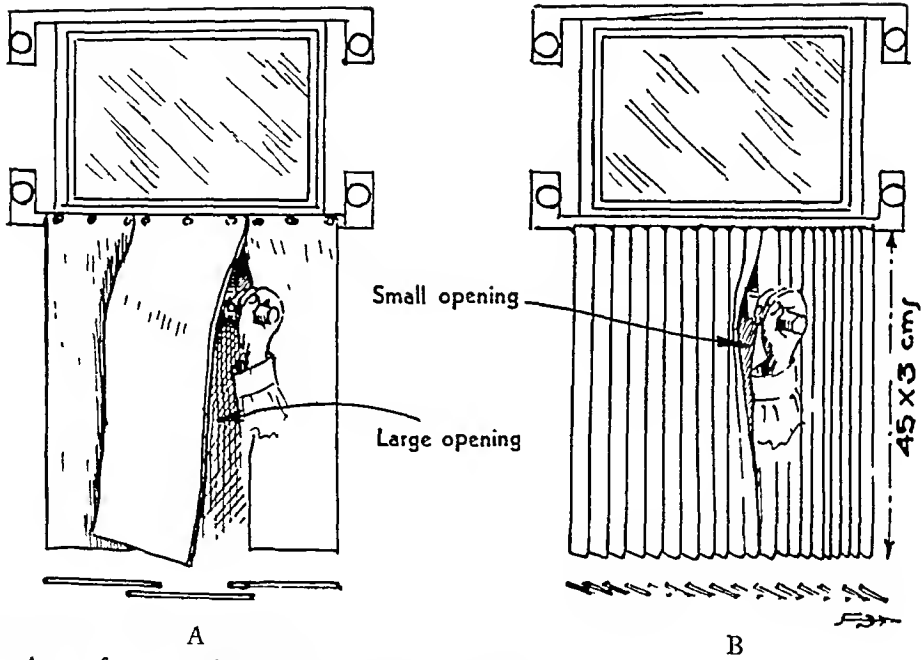


FIG. 2. Apron for protection against secondary radiation. *A*, current model; *B*, Ingber's model. Sketch of the roentgen field according to Ingber



FIG. 3. First phase. Simple diffuse localized compression showed the presence of a niche from ulcer of the lesser curvature of the stomach but failed to show the interruption of the fold mucosa at the base of the niche, an element in roentgen diagnosis which has pathognomonic value.

FIG. 4. Second phase. Controlled compression with Holzknicht's spoon made it possible to demonstrate not only the presence of the ulcer niche but also the lack of continuity of the gastric fold at its base.



FIG. 5. Third phase. Controlled compression with Holzkecht's button near the base of the niche makes better filling of it possible and shows its "penetrating" character.

exercises pressure, but is quite useless because it covers the compressed zone and permits of observation only of the periphery and not of the center of the region under compression which is to be examined.

These two instruments are quite distinct from a poor imitation which is on sale in this country and which uses the name of Holzkecht illegally.

Many years of experience in the obscure field of gastrointestinal roentgen diagnosis has made us realize the inconvenience of



FIG. 6. Fourth phase. Controlled compression with Holzkecht's button in the act of focusing the niche with the greatest possible roentgen precision.

interrupting the examination when it was necessary to use first one and then the other of the above-named instruments and the one which was not being used for the moment had to be laid down and the other felt for blindly.

The *universal distinctior of Holzkecht-Ingber*, which we brought from Europe, unites in a single instrument both these needs of roentgen diagnosis.*

Both instruments are suspended by small

* This device is being manufactured by Lutz and Ferrar's of Argentina.

FIG. 7. *A* and *B*, imitation which is on sale in Argentina and which in reality does not serve the purposes which it claims. 1, the universal distinctior of Holzkecht-Ingber unites in a single instrument the spoon and button for roentgen palpation. 2, very light hollow sleeve of aluminum which, according to Holzkecht's original idea, perfectly meets the anatomical functional demands of the hand which is practicing palpation. 3, only the left hand needs the protective glove. 4, the right hand of the examiner, because of the construction of the instrument, is protected by the lead glass of the screen. 5, palpation is begun with the spoon inserted. 6, when the button distinctior is required, roentgenoscopy is interrupted for a moment. 7, between one examination and the next the instrument is hung around the neck of the examiner with the sleeve resting on his left forearm.





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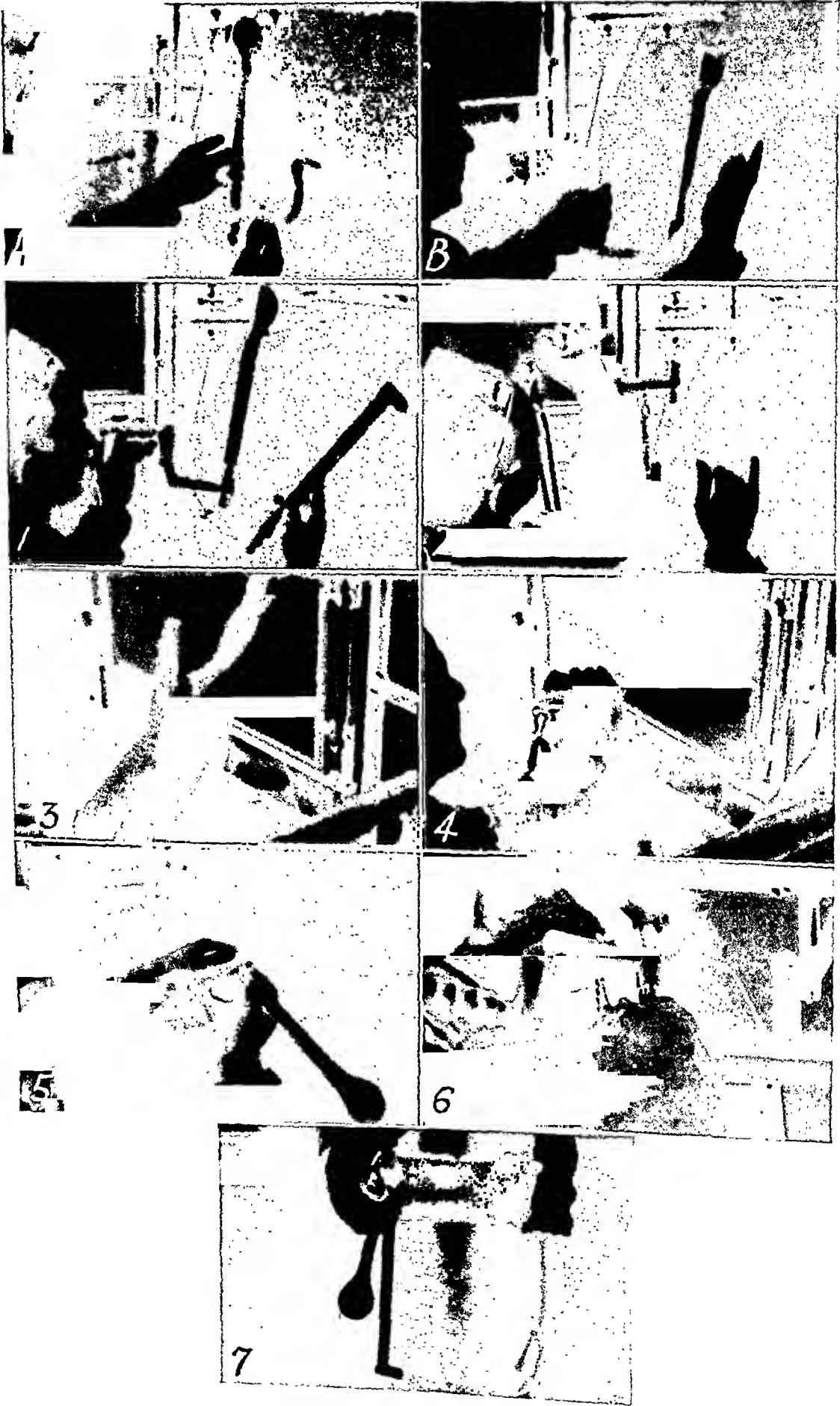
interrupting the examination when it was necessary to use first one and then the other of the above-named instruments and the one which was not being used for the moment had to be laid down and the other felt for blindly.

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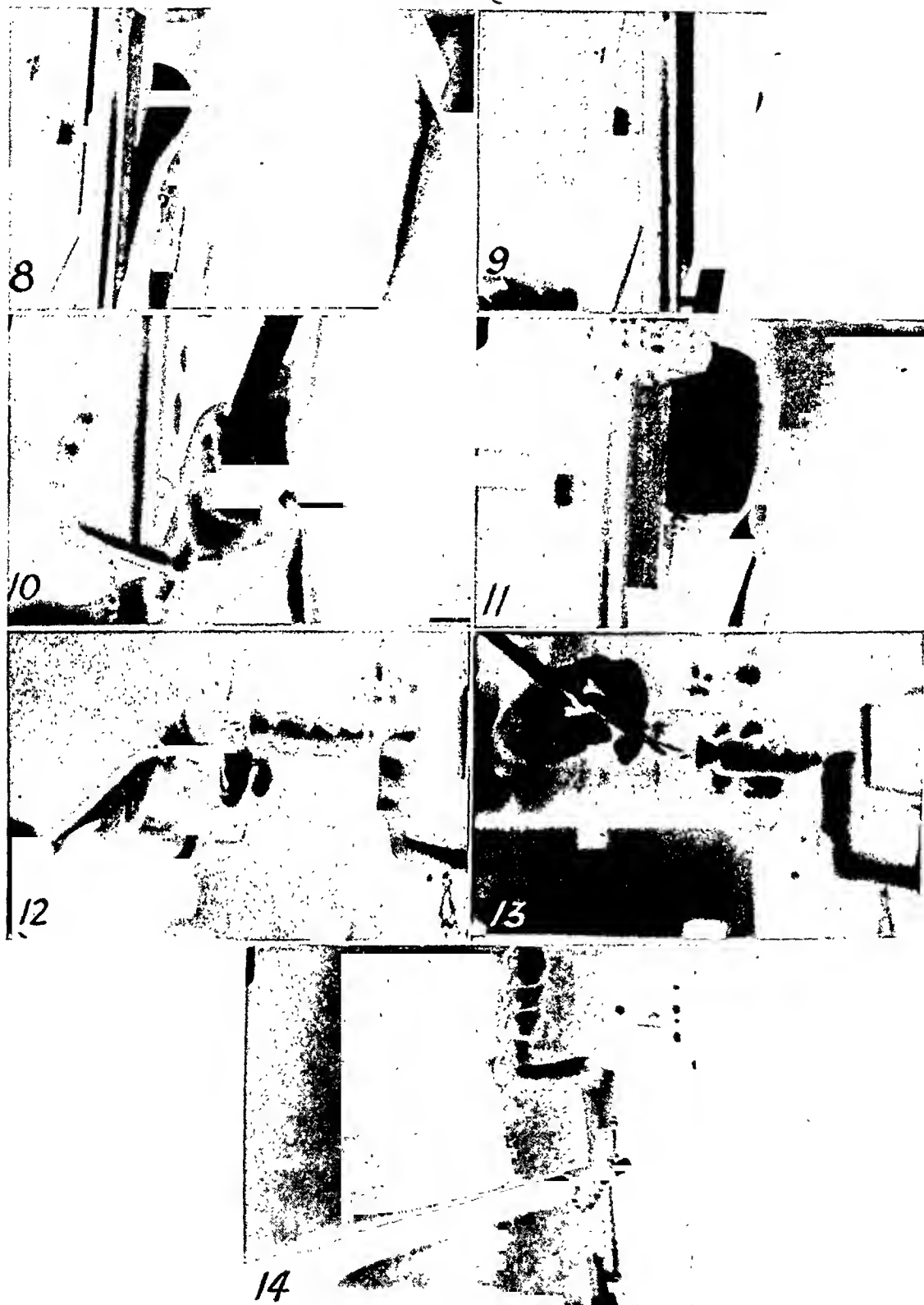


FIG. 8. 8, controlled, local and circumscribed compression with the spoon. 9, same with the button. 10, the patient himself aids in keeping the distinctior in the required position. 11, roentgenography with controlled, local and circumscribed compression. 12, the cord is detached from the sleeve of the distinctior. 13, the cord is reattached to the sleeve of the distinctior. 14, suspended by the cord around the neck of the examiner at the proper time, the distinctior hangs free over the apron of the examiner, leaving both hands free.

chains from a very light hollow sleeve of aluminum, modeled faithfully on Holzknecht's original idea, which is perfectly adapted to the technical functional requirements of the hand which is practicing the roentgen palpation; either the one or the other can be inserted into the sleeve by means of a screw; the one which is not being used at the moment remains suspended from the sleeve.

Between one examination and the next the roentgen palpator can be hung around the neck of the examiner, the sleeve resting on his left forearm.

A glove for protection against the roentgen rays is necessary only for the examiner's left hand; the right hand, because of the characteristic construction of the instrument, is protected by the lead glass.

The palpation is begun first with the spoon-shaped distinctior; when the use of the button distinctior becomes necessary, roentgenoscopy is interrupted for a moment, the spoon unscrewed and the button inserted and then the examination, which has been interrupted only for the insignificant time required for this maneuver, is quickly continued.

Sometimes roentgenography of some di-

agnostic sign becomes necessary which can be accomplished only by the use of one of the palpators, with *controlled, local and circumscribed compression* at a given point of the organ under examination. In such a case the patient himself helps to keep the distinctior in the required position; he assumes control of the distinctior while roentgenoscopy is going on; then the red light is quickly lighted, the cord unhooked from the sleeve of the distinctior, the film introduced into the chassis above the distinctior and the patient freed from the compression, during which time the distinctior may hang free from the neck of the examiner, permitting him to use both hands.

In the survey of the subject which we have made this instrument seems to be very little used, but its use by us has proved invaluable on numerous occasions which have presented themselves in the course of years in the practice of roentgenology; it is easy to realize its value on the basis of the diagnostic discoveries made by it, many of which would otherwise have passed unobserved, with serious consequences in diagnosis.

9 de Julio 714,
Cordoba, Argentina.



IMPROVED TECHNIQUE FOR BRONCHOGRAMS*

By MAJOR WILLIAM A. ZAVOD

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SINCE the introduction of iodized oil by Forestier in 1922, lipiodol has been widely used as a contrast medium for roentgenographic visualization of the bronchial tree. Various techniques for bronchograms are in use today. They range from instillation of the oil through a bronchoscope to mere dropping of the oil on the base of the tongue in the hope that it will seek out the pathologic condition and will be recorded on the roentgenogram. The object of a bronchogram is to demonstrate the presence or absence of a pathologic condition anywhere in the lungs, and therefore a bronchogram should produce visualization of all the major branches and their incident pathology in all the lobes of both lungs. It is the purpose of this paper to describe a technique which permits such visualization.

Objection might arise to the method on the ground that superimposition of the bronchial branches of the various lobes will result when the entire bronchial tree is outlined simultaneously, and thus obscure the pathologic condition in the individual lobes. However, four roentgenographic exposures taken in various positions, to be described below, will give perfect visualization of the state of the bronchi in each lobe of both lungs. There is no danger of critical loss of the physiological function of the lungs when only 20 cc. of lipiodol is used. This was investigated by the author spirometrically and will be the subject of another paper to be submitted for publication.

The method has the following advantages: (1) The entire bronchial tree of both lungs is outlined in one sitting. (2) It permits the study of topographical relationships between the various lobes in each lung. (3) Better roentgenograms result since they are not marred by residual lipiodol from previous instillations.

The technique described was employed

in over 200 bronchograms. No failures were encountered; there were no complications or untoward effects.

The procedure will be described in detail since it is upon these details that the success of every bronchogram depends.

The patient is first examined to ascertain that he is not ill with an acute infection or any other disease which contraindicates the procedure. The ordinary chest roentgenogram, which is a prerequisite to a bronchogram, is studied in attempt to evaluate the presence of pathology. The patient is questioned about hypersensitivity to iodine and cocaine. The procedure of bronchography is explained to the patient and he is to be impressed that his cooperation is essential. No food or drink is to be taken by mouth for at least three hours prior to the examination. Non-fixed artificial dentures are to be removed. The teeth are brushed and the mouth and throat are rinsed with an alkaline antiseptic. A sedative of the barbiturate group, such as nembutal or seconal 0.05 to 0.1 gm., is given by mouth one-half hour prior to the procedure.

The following materials are to be prepared on a sterile tray: a French urinary catheter size 16, made of red rubber (radio-paque); a wire stylet having a laryngeal curve at one end; a De Vilbiss spray bottle; 10 cc. Luer lock syringe and laryngeal cannula; laryngeal mirror, head mirror, alcohol lamp; 2 per cent nupercaine and 4 per cent cocaine; 20 cc. lipiodol and some 4 by 4 inch gauze sponges. All boilable materials are to be sterilized, non-boilable objects are to be washed in 70 per cent alcohol.

The patient is seated in a chair, preferably with a head rest. The operator wearing gown and mask, seats himself in front of the patient at a slightly higher level so that he can look down into the patient's larynx. The larynx is examined by indirect laryn-

* From the Chest Section, Woodrow Wilson General Hospital, Staunton, Virginia.

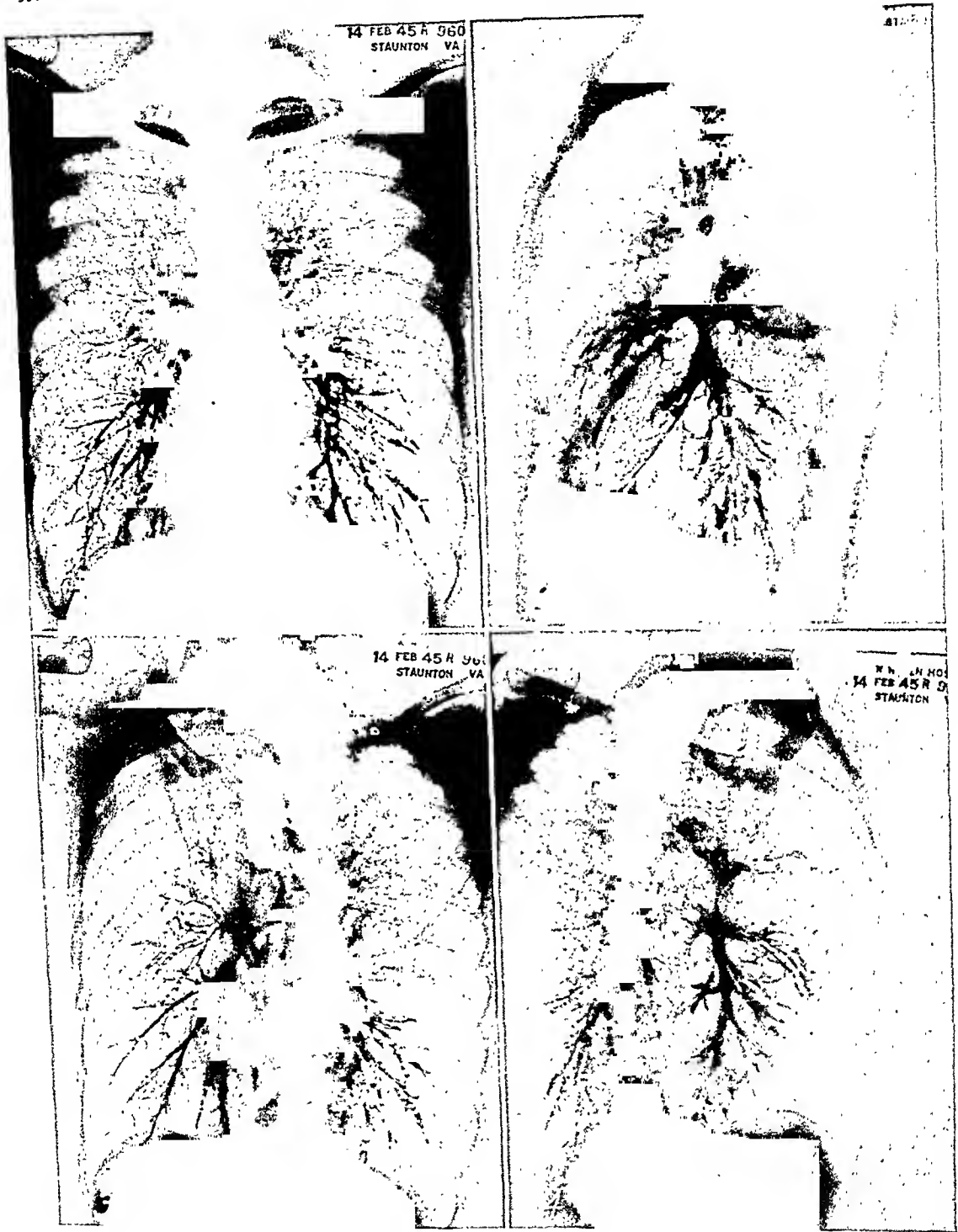


FIG. 1. Bronchogram taken in the dorsoventral position.
FIG. 2. Bronchogram taken in the right lateral position.
FIG. 3. Bronchogram taken in the left anterior oblique position.
FIG. 4. Bronchogram taken in the right anterior oblique position.

gосcopy and any abnormalities are noted. The nasopharynx, including the base of the tongue and the soft palate, is anesthetized with 2 per cent nupercaine by the spray method, about five to eight applications are sufficient to anesthetize these structures.

The larynx, trachea and bronchi are anesthetized in the following manner: The cocaine is drawn up into the syringe and cannula. With the aid of the laryngeal mirror, a few drops of cocaine are placed on the free border of the epiglottis, the interarytenoid space and the true vocal cords. About 1 cc. of cocaine is instilled into the trachea; this will cover the carina and the main bronchi on the right. The patient is now instructed to lean to the left, and while the cannula is between the cords, another 1 cc. is instilled into the left branches. A total of 3 cc. of 4 per cent cocaine is ample for the average patient.

The stylet is introduced into the catheter which takes on the laryngeal curve of the former. Under indirect laryngoscopic vision the catheter and stylet are introduced between the cords and the catheter is fed into the trachea halfway off the stylet. The stylet is now removed from the catheter and a piece of folded gauze is placed between the patient's teeth with instruction to bite on it. This will permit anchoring of the catheter in place without obstructing its lumen.

The patient is now placed in the supine position on the level roentgenoscopic tilt-table, his head on a pillow. The head is turned to the left side and the chest is roentgenoscoped. The catheter is advanced to a position about 2 cm. above the carina. The syringe with 10 cc. of lipiodol is attached to the catheter by means of the cannula and the instillation of oil is begun under roentgenoscopic control. When the oil reaches the intubated end of the catheter, the patient is turned in the oblique position towards the left (right anterior oblique) and the oil will flow down into the left lower lobe. Next, the patient is turned still farther to the left until he is almost in the right lateral position; this will permit the oil to flow into the left upper lobe. It takes about 10 cc. of oil to fill the bronchi of the left lung. The syringe is refilled with another 10 cc. of oil, the patient's head is turned to the right; the left shoulder is raised and the patient is turned slightly to

the right (left anterior oblique). As the oil runs down, it will fill the right upper lobe first; next, the lower lobe is filled and some of the oil will enter the middle lobe. After all the lipiodol is instilled, the catheter is removed. The patient is now told to turn in the prone position and one can visualize roentgenoscopically some of the oil running from the posterior bronchi to fill the anterior branches. Since the entire filling of the bronchi is done under roentgenoscopic control, any abnormalities are readily noted and serve as a check against the roentgenograms to be taken.

Careful roentgenoscopy is as important as the bronchogram. The dynamics of the bronchi are readily observed roentgenoscopically, also abnormalities like partial bronchial block or pooling of the oil can be easily seen, while they do not always show up on the bronchogram.

One must be cautious not to expose the patient to the roentgen ray for too long a period. A frequent momentary flash of the ray on the screen will permit visualization of the gradual filling of the bronchi without overheating the roentgen tube or causing injury to the patient.

With the patient in the erect posture, four roentgenographic exposures are made. A dorsoventral, a right anterior oblique, a left anterior oblique and a right or left lateral view, the latter depending upon the localization of the pathologic condition as it was observed under the roentgenoscope.

Figures 1, 2, 3 and 4 are reproductions of bronchograms made with above technique. Note the complete filling of the main branches of all lobes of both lungs; the demonstration of the pathologic condition and especially the localization of the disease in the posterior portion of the right upper lobe.

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The author wishes to thank Major Donald Gordon, Chief Roentgenologist at the Woodrow Wilson General Hospital for the cooperation of his department.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

PEREIRA DA SILVA, C. and PENHA GODOY D'ALAMBERT, J. Síndrome de hiperostose frontal interna. (Syndrome of internal frontal hyperostosis.) *Arq. assist. psicopat. estad. São Paulo*, March-June, 1943, 8, 101-141.

Internal frontal hyperostosis was first observed by the anatomist Morgagni in the autopsy of a woman who showed obesity and virilism. He wrote two papers on it in 1719 and 1761. The authors review the literature of the subject since that time, giving brief notes of the principal works on the subject.

Their own work consists of a discussion of 14 cases seen at the Juqueri Hospital in São Paulo, Brazil. Eight of the cases were purely clinical and in 6 anatomical as well as clinical examinations were made. Histories of all the cases are given and two tables showing the chief features of the cases in the two groups. The article is also profusely illustrated with photographs and roentgenograms of the patients. The disease is characterized, as its name indicates, by hyperostosis of the internal table of the frontal bone which sometimes extends to the parietal also. Moore classifies it into four groups which, however, are really only different stages of the process. The disease is probably due to a disturbance of calcium metabolism but it is hard to explain why the bone deposit is made only in the internal table of the frontal bone. Intracranial hypertension was found frequently. One patient had an eosinophilic hypophyseal adenoma, one a frontal meningioma involving most of the hyperostotic area and one had syphilis.

The great majority of the patients are women. In women who present obesity, headache, menstrual disturbances and hypercalcemia roentgen examination should be made for this disease. Four of these patients had epilepsy. As the material was from a hospital for mental diseases the significance of mental symptoms could not be judged.—*Audrey G. Morgan.*

HOLVEY, ERVIN H., and ROSENTHAL, LOUIS M. Tomography in the region of the maxillary sinuses. *Radiology*, May, 1944, 42, 458-465.

The object of this article is to compare the normal tomographic findings in the maxillary antra with the findings in disease. A series of tomograms were made at 0.5 cm. levels through the head of an adult cadaver in the antero-posterior projection. These are presented, together with tomograms taken in cases of infection of the sinuses and of carcinoma. Tomograms of infection show dense opacity of the antrum but the process does not involve the walls. This lack of involvement of the bony walls is most important in diagnosis. The antral cavities are symmetrical. The pathologic process generally extends to the adjacent ethmoid sinuses and there is practically always edema of the adjacent turbinates and the nasal mucosa.

In cancer of the antrum the bony walls of the cavity are invaded, a differentiating sign from inflammation. The soft tissue shadow of the growing tumor extends beyond the bony walls and invades neighboring structures, such as the naris, orbit and mouth. The ethmoid sinuses are frequently invaded. The thin lower wall of the orbit explains the frequent extension to the orbit of cancer of the antrum.

Ordinary roentgenograms often fail to show the cancerous invasion of the bony walls of the antrum. Usually the patient does not come for medical advice until the cancer has destroyed the bony walls of the cavity and caused nasal obstruction, visual disturbance or pain by its expansion. If there are such symptoms and the ordinary roentgenograms suggest the possibility of cancer in this region a tomographic study should be made.—*Audrey G. Morgan.*

MAGUIRE, DANIEL L., JR., and KALAYJIAN, BERNARD S. Unusual stab wound. *Radiology*, July, 1944, 43, 65-67.

The unusual feature of this case is that a part of a knife blade remained in the deep tissues of the face for four months without being discovered.

The patient was a colored man, twenty-seven years of age, who was stabbed in a quarrel in April, 1942. There was a small laceration about an inch long in the middle of the left zygoma. Probing did not show any foreign body and the lesion was cleansed and sutured; healing was by first intention and the patient was discharged five days later without pain, swelling, redness or fever. About four months later he returned to the hospital complaining of pain and stiffness in the jaw. It grew worse until he could open the jaw only about an inch and had to live on liquids entirely. No history of chills, fever, swelling, localized tenderness or drainage from the site of the injury.

Multiple roentgenograms of the skull and jaw showed a knife blade about $2\frac{1}{2}$ inches long and $\frac{1}{2}$ inch wide in the soft tissues of the left side of the face, extending medially and slightly downward and forward from a point just below and medial to the left zygomatic arch. Roentgenograms of the skull with the knife blade in situ are given.

The knife blade was removed. A small bent tip had broken off and remained in the wound. It was thought unwise to probe for it and it was not believed that it would cause any further trouble. The wound healed by first intention and in about a month the patient was able to open his jaw completely and eat all kinds of food. A year later he had had no further trouble.—*Audrey G. Morgan.*

NECK AND CHEST

HANKINS, WALTER D. Traumatic hernia of the lateral pharyngeal walls. *Radiology*, May, 1944, 42, 499.

A case apparently unique in medical history is described. The patient was a trumpet player in the regimental band admitted to the Station Hospital at Fort Banks, Mass., for psychiatric examination. A bulge the size of an egg was seen in the right cervical region which appeared when the patient blew his trumpet. About six months before while playing his trumpet he felt something "give way" on the right side of his neck and ever since that time this bulge had appeared when he blew his trumpet. Roentgen examination showed that the lateral walls of the pharynx were herniated. The posterior wall was also weakened and bulged posteriorly upon the esophagus. The apices of the lungs rose above the clavicles and in the lateral view can

be seen superimposed on the lower part of the trachea. Anteroposterior and lateral views of the case are given.—*Audrey G. Morgan.*

LAVNER, GERALD, and COPLEMAN, BENJAMIN. The antero-posterior lordotic projection in the roentgenographic examination of the lungs. *Radiology*, Aug., 1944, 43, 135-141.

In some cases the usual roentgenographic examination of the chest does not show small lesions in the apices of the lungs. The authors describe the anteroposterior lordotic projection used in the demonstration of such lesions. The examination may be done rapidly with the use of only one 10×12 inch film. The patient faces the tube and with the knees slightly bent and the abdomen protruding in extreme lordosis leans backwards against the cassette holder. The central ray is directed horizontally. The technical factors used are such that the exposure is twice that for the routine posteroanterior projection at 6 feet; or the same factors are used as in the ordinary examination and the distance decreased to 4 feet.

This position causes the clavicles to be projected upwards while the anterior portions of the ribs become practically horizontal. This projection has proved most useful in cases in which there is only a suspicion of a shadow behind the clavicles.

Photographs of a patient in position for examination and roentgenograms of illustrative cases are given.—*Audrey G. Morgan.*

ZANCA, PETER, and HERPEL, FREDERICK K. A statistical analysis of 100,000 examinations of the chest by the photoroentgen method. *Radiology*, Aug., 1944, 43, 122-128.

Tables are given showing the results of routine examination of the chest by the photoroentgen method of 100,000 selectees reporting to the Armed Forces Induction Station at Fort Bragg, North Carolina. Heretofore routine chest examinations have been made with stereoscopic 14×17 inch films but the authors find that the photoroentgen method with 4×10 inch films is better. It is much cheaper and the films can be read and interpreted much more rapidly. Besides, the sharpness and definition of the image is greater on the smaller films. Superior films are produced by the use of a Lysholm grid in front of the intensifying screen. The rejection rate for pulmonary tuberculosis

in this series of cases was 4.91 per thousand. This included all types of tuberculosis from advanced to apparently arrested cases. This is a very low rate as compared with that in the country as a whole which for the period from November, 1940 to December, 1941 was 11.06 per thousand. This low rate is doubtless due in part to the splendid antituberculosis campaign that has been carried on in North Carolina for the past twenty-five years, in part to the fact that known cases of tuberculosis were screened out by the local boards and in part to the fact that most of these draftees were from rural regions.—*Audrey G. Morgan.*

WARING, JAMES J., and SCHMIDT, ERNST A. Esophagocecal fistula diagnosed roentgenologically. *Radiology*, July, 1944, 43, 59-62.

As no similar case is known in the literature the authors report a case of stricture of the esophagus in a woman of forty-five caused by swallowing lye. She came to the Colorado General Hospital March 4, 1943, complaining of loss of weight and strength and inability to retain food. She said she did not always regurgitate her food, which was entirely liquid, and she was sure some of it passed into her stomach. In about three-quarters of an hour she had several loose stools which resembled the food just swallowed. There were none of the usual eye and mouth signs of vitamin deficiency. She had pain in the right loin and walked with a distinct limp, which suggested iliopsoas spasm. Apparently successful dilatation of the esophagus had been done but she did not gain in weight and this fact, in conjunction with the flushing of the bowels and pain in the loin, suggested esophageal fistula.

The first roentgen examination March 11, 1943, showed a fistulous tract extending from the esophagus into the abdomen and a further examination in April showed that the fistula extended into the cecum. It was surrounded by a mass of gristly white tissue. There had been no marked symptoms to show when the perforation occurred. A gastrostomy was performed on April 30 and nine days later death occurred from peritonitis and bronchopneumonia; death was entirely independent of the esophageal and cecal lesions. An appendectomy had been performed recently and it is not known whether it had anything to do with the perforation of the fistula into the cecum.—*Audrey G. Morgan.*

PETERSON, VERNON L. Fungus disease of the chest. *Radiology*, July, 1944, 43, 14-20.

The author discusses a group of lung infections caused by *Coccidioides*, *Actinomyces*, *Aspergillus*, *Monilia albicans*, *Torula* and *Blastomyces*. In about one-fourth of these cases there was fungus infection elsewhere in the body and this is an aid in the differential diagnosis of the lung lesions. Both the clinical and roentgen findings are similar to those of tuberculosis so that differentiation is difficult. However, though a diagnosis cannot be based on a single roentgen examination there are certain features which appear on repeated examinations which aid in diagnosis if the roentgenologist is familiar with them. These findings are briefly discussed for the different groups of fungus infection and illustrated with roentgenograms. In lesions that look like tuberculosis but in which no tubercle bacilli can be found, a very careful search for fungus infection should be made. If no fungi can be isolated a therapeutic test with iodides may be made; a positive response indicates fungus infection.

All of the cases of coccidioidomycosis were from the southwestern United States, most of them from California. Several had a history of a fever resembling influenza that was doubtless "valley fever." There was little clinical evidence of disease in any of them.

Doubtless many cases of fungus infection will be seen as the men return from the Army camps. It is important that these lesions be recognized and differentiated from tuberculosis or other more serious diseases as the course of the fungus infections is usually benign and it will not be necessary for the patients to give up their work.—*Audrey G. Morgan.*

JOHNSTON, WAYNE A., and HEYDEMANN, JULIUS. Clinical and radiological studies in pulmonary mycosis. *Radiology*, July, 1944, 43, 1-13.

Only a small number of yeast fungi are pathological to animals and man. Their classification is extremely difficult and the authors think it better to consider diseases caused by them from the point of view of their virulence rather than from that of the species of fungus causing them. Susceptibility seems to be influenced by whether the region is infected or non-infected rather than by any personal characteristics of the patient, such as age, sex

or occupation, though blastomycosis seems to occur more frequently in men who handle cattle.

The symptoms do not differ strikingly from those of other lung infections. The clinician will note that there is some type of lung disease, the roentgenologist can learn its extent and distribution but the final diagnosis must be made by demonstration of the fungi in sputum cultures. At present it is often not recognized until a late or terminal condition has developed. The authors urge research to find a means of differential diagnosis of these infections early in their course.

Roentgen differentiation of fungus infection from tuberculosis is not reliable. The two diseases may coexist and the mere finding of yeast fungi does not prove that the patient does not have tuberculosis. This should be borne in mind in treatment.

The best treatment for mycosis of the lungs is iodides and roentgen irradiation. In moniliasis and blastomycosis it may be necessary to desensitize the patient to the yeasts before he is given iodides. This is done by giving Lucas vaccine, 0.1 cc. twice a day, increasing to 0.8 cc. for a total of eighteen injections.

Eight cases are reported in detail and illustrated with roentgenograms and photomicrographs of lung tissue.—*Audrey G. Morgan.*

LEVENE, GEORGE, and STERMAN, IDA A. Roentgen study of primary atypical virus pneumonia. *Radiology*, May, 1944, 42, 446-457.

Small epidemics of virus pneumonia have been prevalent in this country since 1935. It is probably caused by a filtrable virus. The disease has not been transmitted to animals.

The authors made a roentgen study of 100 consecutive cases in the Department of Radiology of the Massachusetts General Hospital. Roentgenograms of the various stages of the disease are presented. The first lesion visible roentgenologically is a severe tracheobronchitis. The process is destructive and quite different from the inflammatory exudates seen in pneumococcal pneumonia. In the comparatively few autopsied cases the lungs were red and edematous. There were small areas of focal or lobular atelectasis and areas of emphysema. The emphysema prevented total lobular atelectasis so that consolidation was generally not uniform. During the course of the disease the roentgen appearance may vary greatly and may simulate

tuberculosis, lobar pneumonia, bronchopneumonia, abscess, bronchiectasis, metastatic carcinoma or pulmonary edema. It may be necessary to base the diagnosis on the history, clinical and laboratory findings and serial chest roentgenograms.

Resolution progresses from the periphery toward the center, unlike that of pneumococcal pneumonia. The average duration of symptoms on admission in these cases was seven days. There were visible roentgen changes at this time. It has been stated that the first roentgen changes appear on the fourth day. In this series the average time for the beginning of resolution was on the seventeenth day and that for return to normal the twenty-fifth day. Roentgen signs may persist long after clinical cure, suggesting the possibility of chronic complications, particularly bronchiectasis. It is therefore advisable to take a roentgenogram on the day of discharge and another some time later if there is any indication for it.—*Audrey G. Morgan.*

EHRLICH, DAVID E. Aortic arch and cardiac mensuration. *Radiology*, April, 1944, 42, 382-383.

The author describes a simple method of measuring the heart and aortic arch which he has found satisfactory in over twenty years' experience.

A routine posteroanterior roentgenogram is taken at 6 feet distance with the patient standing facing the film and in full inspiration. After dark-room processing a midline is drawn by dropping a plumb line through the posterior spinous process of the mid-cervical vertebrae. Next a horizontal line is drawn at the level of the cardiophrenic angle. The transverse diameter of the chest is measured along this from the inner rib borders on each side. The distance from the midline to the right and left borders of the heart is then measured. The sum of these two distances gives the transverse diameter of the heart. The ratio of this to the transverse diameter of the chest is figured out. The measurement of the aortic arch is obtained by measuring the greatest distance from the midline to the left, which roughly approximates a 10:1 ratio to the transverse diameter of the chest. This eliminates the need of hunting for the right margin of the aortic arch which is often hidden behind the sternum.—*Audrey G. Morgan.*

DEWEESE, E. R., and HOWARD, JOHN C., JR.
Congenital absence of a lung diagnosed before death. *Radiology*, April, 1944, 42, 389-391.

Congenital absence of the lung is considered rare. Only 38 authenticated cases have been reported since the first one in 1787. Only 3 of these cases were diagnosed before death. One lung functioning normally is sufficient for life as shown by the fact that 11 of these patients were over 20 years of age and one was 65. The increased use of routine chest plates in the armed services will without doubt reveal many more of these cases.

One is described in a boy 6 months of age. This is the second case seen in the Children's Mercy Hospital, Kansas City, Mo. in the past 6 years. Both were diagnosed during life. This patient was admitted with a diagnosis of acute bronchitis, pharyngitis and atelectasis of the right upper lobe. Roentgen examination showed a dense homogeneous opacity over the entire right lung field with great displacement of the mediastinal structures to the right. The heart lay entirely to the right side of the vertebral column. There was over-aeration of the left lung which extended across the right side of the chest. On bronchoscopic examination no opening of the right main stem bronchus could be found. Obviously no air was entering the right lung. A diagnosis of agenesis of the right lung was made. The child died three days later and autopsy confirmed the diagnosis. It should be possible to make a diagnosis of this condition during life by the use of roentgen examination, lipiodol injection and bronchoscopy.—*Audrey G. Morgan.*

STEIN, GEORGE H., and KRESKY, PHILIP J.
Comparative roentgen study of primary atypical and bacterial pneumonia. *Radiology*, May, 1944, 42, 435-445.

Various writers on the subject have attempted to describe roentgen pictures of atypical and bacterial pneumonias which would serve to differentiate the two types of disease. The authors made a study of 2,062 cases of pneumonia seen at the Regional Station Hospital in Sioux Falls; 950 were bacterial pneumonias and 1,112 were primary atypical pneumonias. For purposes of comparison they have selected 19 cases of the two types and give clinical histories and roentgenograms.

From a careful study of these it is evident that it is impossible to make a diagnosis of the etiology of a given case of pneumonia from the roentgenogram alone. Cases of primary atypical pneumonia may show a roentgen appearance that cannot be distinguished from that of pneumococcic pneumonia, especially in the early and resolving stages of the latter. Contrary to most of the descriptions in the literature, they saw many cases of atypical pneumonia which did not originate in the hilar regions and extend outward but occurred as circumscribed foci in the periphery of the lung. They also saw primary atypical pneumonias which occurred in the upper lobes with roentgen findings resembling those of tuberculosis.

Any accurate differentiation between the two types of pneumonia must take into consideration the clinical and laboratory findings as well as the roentgen appearance.—*Audrey G. Morgan.*

LEWIS, ELBERT K., and LUSK, FRANK B.
Roentgen diagnosis of primary atypical pneumonia. *Radiology*, May, 1944, 42, 425-434.

Atypical pneumonia is a virus disease, which may be of known etiology, as influenza A or B or psittacosis, or of unknown cause. The author discusses 6,000 cases of acute epidemic infection of the respiratory tract seen at the Station Hospital, Fort Custer, Mich. Of 500 such patients studied in detail about 25 per cent showed roentgen evidence of atypical pneumonia.

Atypical pneumonia shows four phases. The first or bronchitic phase is characterized by increased size and density of one or both hilar shadows and prominence of the truncal shadows extending from the hila into the lower lobes. This phase must be differentiated from acute and chronic bronchitis and passive congestion and enlargement of the hilar nodes from any cause. The second or peribronchitic phase shows increased prominence of the truncal markings extending downward into the lower lobes and outward into the lung parenchyma. This is the phase most likely to be confused with bronchiectasis. In the third or alveolar phase the lesion varies in size, location, shape and density. Usually it extends from the hilum outward and downward into the lower lobes. The roentgen shadow varies from the size of a millet seed to involvement of the greater part

of a lobe. Because of the great variability in the shadow this phase must be differentiated from many other lung conditions, such as the bacterial pneumonias, especially the lobar type, tuberculosis, atelectasis, pulmonary abscess, encapsulated fluid, tumors and rickettsial and fungus infections. The fourth or broncho-alveolar phase shows irregular, soft, patchy mottled areas of increased density in the lung parenchyma. It must be differentiated from bacterial bronchopneumonia, the rickettsial and fungus infections, tularemia and measles pneumonias and occasionally infected bronchiectasis.

Roentgenograms of these different phases and photomicrographs of the histopathological findings are given. The roentgen appearance alone, however, is not enough for differentiation but the clinical and laboratory findings must be taken into consideration.—*Audrey G. Morgan.*

LOWRY, THOMAS, and RIGLER, LEO G. Adenoma of the bronchus: a clinical and roentgenologic study with a report of seven cases. *Radiology*, Sept., 1944, 43, 213-229.

Malignant tumors of the bronchi are very frequent; benign bronchial tumors are much less common but not rare. About 80 per cent of the group of benign growths are adenomata. It is important to differentiate these from carcinoma as they require less radical treatment. While adenoma is classified as a benign tumor it is locally malignant in the sense that it invades beyond the wall of the bronchus and there is often an extrabronchial mass. This is due to the fact that this form of tumor probably originates from the duct epithelium of the bronchial mucous glands and the mucous ducts penetrate the cartilaginous rings. But it does not produce malignant metastases and in this sense may be said to be clinically benign.

Differentiating signs between adenoma and carcinoma are that 80 per cent of adenomata occur in patients less than forty years of age while 90 per cent of carcinomata occur in subjects over forty; 70 per cent of adenomata are in females while 85 per cent of carcinomata are in males; on bronchoscopy the adenoma is a smooth, pink, oval or lobulated mass, often pedunculated; the bronchus is not fixed. Troublesome bleeding is produced on biopsy. Carcinoma is irregular, yellowish or gray, often ulcerated; the bronchus is infiltrated and fixed. On biopsy there is not profuse hemorrhage. In

adenoma bronchiectasis is frequent, due to the slow course of the disease, while in carcinoma it is rare as the disease is rapidly progressive. Hemoptysis is often profuse in adenoma, beginning and ending abruptly, while in carcinoma it is usually only streaking and often continuous.

If the clinician has bronchial adenoma in mind a diagnosis can generally be made by roentgen examination and bronchoscopy. A patient with a chronic productive cough, recurrent hemoptysis and fibrocavernous destruction of one upper lobe, whose sputum is negative for tubercle bacilli should be examined for bronchial adenoma by all possible means including body section roentgenography, which often permits of direct visualization of the tumor as a rounded, sharply defined dense shadow in contrast with the air in the bronchus which surrounds it.

Local bronchoscopic removal may be used in the treatment of these tumors in young patients whose lung shows little damage and who can be closely followed up. Irradiation has not proved of great value and there is a risk of death from hemorrhage due to deep necrosis of the bronchial wall eroding large vessels. Resection of the lung is indicated in a large majority of the cases but the advantages to be gained must be weighed carefully as compared with the very considerable danger of the operation. Seven cases are reported and illustrated with roentgenograms.—*Audrey G. Morgan.*

KRAFT, ERNEST. Lung abscess secondary to stenosing bronchiogenic carcinoma. *Radiology*, July, 1944, 43, 39-47.

Pulmonary carcinoma now causes 10 per cent of all carcinoma deaths. In addition to an actual increase there is an apparent increase due to more thorough roentgen examination and greater familiarity with the picture. It is believed that as many as 90 per cent of cases could be recognized with proper examination and two-thirds of cases from roentgenograms alone. There are two reasons why many cases are still unrecognized: (1) when the lung tumor remains asymptomatic distant metastases may be mistaken for the primary tumor; (2) stenosing bronchiogenic carcinoma, which is the most common form, is usually masked by infections of the surrounding lung and pleura.

Stenosing bronchiogenic carcinoma can be cured if diagnosed early. Histologically it is a

squamous-cell growth and is much less malignant than the adenocarcinomas and small-cell sarcomas which develop outside the bronchi. Death is usually caused not by the tumor but by secondary changes in the lung. When the obstruction of the bronchus remains complete secretion accumulates on the distal side of it and causes bronchiectasis; secondary infection then causes chronic pneumonia, lung abscesses or pleurisy. The tumor may become so necrotic as a result of these secondary changes that it practically disappears and can only be recognized on careful microscopic study. It is very important for roentgenologists to know of these abscesses secondary to stenosing bronchiogenic carcinoma for if diagnosis is made promptly radical surgery may save the patient's life.

Three typical cases of lung abscess secondary to stenosing bronchiogenic carcinoma are described and illustrated with roentgenograms. —*Audrey G. Morgan.*

ROWLAND, DRIVER. Cardiac aneurysm; Report of a case with correlation of clinical, radiological and electrocardiographic findings. *Ann. Int. Med.*, August, 1943, 19, 349-356.

A case is reported and a review of the literature is given. About 85 per cent of ventricular aneurysms are said to follow cardiac infarction subsequent to the occlusion of a coronary artery. The balance is made up of miscellaneous causes such as syphilis of the myocardium or is of mycotic, traumatic, congenital and traumatic origin. Subsequent to the occlusion of a coronary vessel there appears necrosis of the myocardium supplied by this vessel with replacement fibrosis. This weakened area then stretches with the production of a large or small aneurysmal dilatation, depending on the size of the area involved. This may be saccular in outline communicating with the ventricular cavity by a neck or more often a bulge or out-pouching, not sharply delineated, of the ventricle. An aneurysm may be located in any part of the left ventricle. Aneurysms of the right ventricle are rare but the most common site is the anterior wall involving the apex of the left border just above the apex.

Clinically there is nearly always a past history of coronary occlusion. An enlarged heart is characteristic but this alone is without significance unless it occurs in a patient who was previously known to have no cardiac condition that would explain this enlargement.

Pulsatory phenomena have been of great diagnostic significance. Roentgenography, more especially roentgenoscopy, offers the best means of accurately diagnosing cardiac aneurysm. The following roentgenographic signs are said to be of diagnostic significance: (1) enlargement of the left ventricle with deformity of its contour; (2) a localized protuberance inseparable from the heart shadow on rotation of the patient; (3) abnormal or absent pulsations of the aneurysmal zone; (4) evidence of adhesions between the heart and the chest wall; (5) calcification of the wall of the sac or contained clot. There are three significant changes to be noted upon roentgenoscopy: (1) a diminished or total lack of pulsation in the region of this bulge; (2) a paradoxical pulsation in the region of the supposed aneurysm, i.e. a systolic expansion of this area; (3) calcification of the pericardium or wall of the aneurysm.

In view of the rarity of occurrence of right axis deviation in cases with hypertensive or arteriosclerotic heart disease and of its frequency (40 per cent of cases) in cardiac aneurysm, it is believed that this type of electrocardiogram is very suggestive of a cardiac aneurysm and when it occurs unexpectedly in a case of otherwise unexplainable left ventricular enlargement the possibility of this diagnosis should be brought to mind.—*J. J. McCort.*

MILLER, HENRY. Spontaneous mediastinal emphysema. *Ann. Int. Med.*, Dec., 1944, 21, 998-1010.

A short résumé of the causes of mediastinal emphysema from the literature is given. Certain characteristic physical findings indicative of pneumomediastinum are said to have been described by Muller in 1888. There are: (1) the presence over the precordium of bubbling crepitation synchronous with the heart beats, (2) the disappearance of cardiac dullness, (3) the appearance of subcutaneous emphysema. The diagnosis in most cases is not difficult when the distinctive sounds heard over the heart and the roentgenographic evidence of air in the mediastinum are present. In this paper 4 additional cases of spontaneous mediastinal emphysema are added to the literature of those previously reported. In each case the diagnosis was made by the detection of the typical sounds over the heart. The diagnosis was confirmed by roentgenographic study. It is pointed out that the heart sounds show great variation in in-

tensity and quality during the course of the condition. They may be detected after the appearance of spontaneous pneumothorax and may last for several weeks.

The experimental studies made by Macklin (*Arch. Int. Med.*, 1939, 64, 913-926) on the pathologic physiology are quoted in detail. By artificially increasing the intrapulmonary pressure in the lobe of the lung of cats and other animals he was able to demonstrate that the air enters the perivascular sheath of the finer branches of the pulmonary vessel, presumably through the numerous minute ruptures in the walls of the alveoli. As the increased pulmonary pressure continues, the small bubbles of air coalesce into large ones as they move towards the roots of the lungs through the artificially produced channels in the vascular sheaths. At the root of the lung the air bubbles may merge into large blebs which can impede the pulmonary circulation. Further leakage causes these blebs to break through into the mediastinum. At times the air in the perivascular sheaths may extend into the adjoining connective tissue and dissect a pathway towards the pleura where it forms a subpleural bleb, particularly in the region of the root of the lung. Rupture of this bleb may occasionally produce a pneumothorax.

The paths of extension of air in the mediastinum have also been studied. The air tends to follow with predilection the fascial planes, particularly the sheaths surrounding blood vessels. It may spread upward into the root of the neck, the face, axilla, anterior chest wall, and arms. It is possible for it to dissect up along the sides of the trachea to the floor of the mouth extending under the base of the tongue which becomes elevated. It may extend forward between the parietal pleura and pericardium to appear as blebs overlying the heart, laterally into the opposite lung and downward into the retroperitoneal space where it may outline the kidneys, ureters and renal vessels.

Roentgenographic demonstration of air in the mediastinum is diagnostic. In the anteroposterior view only the outlined pockets of air may be seen, so that lateral and oblique views should also be taken. In these views air may be visible between the heart and the posterior chest wall or in the posterior mediastinum. In rare cases when the air does not extend forward around the heart the characteristic auscultatory signs may be absent and the roentgeno-

graphic evidence of air in the mediastinum may be decisive. Air may also be detected in the subcutaneous tissues of the neck and in the retroperitoneum.

An additional case is reported in which pneumomediastinum followed postoperative massive atelectasis of the right lung. In this case it was believed to be due to over-distention of the left lung. The alveolar ectasia in the left lung permitted the air to escape into the perivascular sheaths and lead to mediastinal and subcutaneous emphysema.—J. J. McCort.

ROBBINS, LAURENCE L. The roentgenologic features of mediastinal tumors. *Radiology*, Aug., 1944, 43, 115-121.

From 1938 through 1942, forty-four cases of proved mediastinal tumor were seen at the Massachusetts General Hospital. They are discussed with a view to determining whether they can be classified by roentgen examination before operation. No absolutely diagnostic signs of the different types were found but certain roentgen signs aid in differentiation.

Among the chief types the bronchiogenic cysts show a smooth round or ovoid shadow anywhere in the mediastinum, with no evidence of bone erosion or calcification. They may be attached to the trachea but other pathologic masses may also. Unless the cyst becomes infected it is usually found incidentally.

All of the dermoid cysts were in the anterior mediastinum. The outline was more irregular than that of the bronchiogenic cysts. Three of the 7 cases showed calcification in the wall, one with actual bone formation. The three teratomata were also in the anterior mediastinum. Two showed slight lobulation, the third was smooth; all were homogeneous in density. The neurogenic tumors included 10 neurofibromata, 2 ganglioneuromata and 2 neuroblastomata. They were in the posterior mediastinum in 9 cases and in the anterior in 5 cases. They were all smooth in outline and homogeneous in density. They showed bone erosion from pressure but no malignant invasion of bone. One unclassified malignant tumor showed slight lobulation with some atelectasis in the lung and a small amount of fluid in the pleural cavity.

Intrathoracic goiters are attached to the trachea. There was only one parathyroid tumor in the right upper mediastinum; it was a smooth mass with no special roentgen charac-

teristics but diagnosis was aided by the fact that the patient showed hyperparathyroidism, both clinically and roentgenologically. One benign thymoma in the anterior mediastinum cast a shadow overlying the pulmonary artery for which it was mistaken.—*Audrey G. Morgan.*

ALEXANDER, THEODORE O. Irradiation pneumonitis. *Bull. Johns Hopkins Hosp.*, Oct., 1944, 75, 199-208.

This report concerns a fifty-two year old white male who was admitted to Johns Hopkins Hospital January 14, 1939 and who died September 28 of the same year. A diagnosis of Hodgkin's disease was made by biopsy of an axillary gland and roentgen examination of the chest showed widening of the mediastinum due to enlargement of lymph glands, and pulmonary infiltration more marked on the left side. Between January 21 and the date of death he received extensive roentgen therapy to various sites of involvement. His chief symptoms throughout were indicative of pulmonary involvement and though a good response was obtained to therapy over the mediastinum in the first five months of his illness, treatment was ineffectual thereafter and he died because of inability to sufficiently ventilate his lungs.

Between January 21 and March 1 he received 1,050 roentgens to anterior and posterior mediastinal fields, the lung fields being shielded. Between April 26 and May 4 he received an additional 420 r to these fields under similar conditions. From July 6 to September 28 he was treated over the mediastinum and lung fields, without shielding, 400 r to the lower right thorax, 2,261 r to the posterior mediastinum and 1,818 r to the anterior mediastinum—the total dosage of radiation without shielding of the lungs was, thus, 4,479 r given in approximately eleven weeks.

At autopsy there was no evidence of Hodgkin's disease in the lungs, though there were large, deep-staining Dorothy Reed cells in minute foci in the bronchial lymph nodes. The lungs showed characteristic lesions due to over-irradiation such as have been described following animal experiments by Davis, McIntosh and Spitz, and Warren and Spencer. Grossly there were consolidated areas in both lungs and within the consolidation grayish-yellow areas of infiltration. Microscopic sections of both lungs "showed large groups of involved alveoli between which the tissue appeared unaffected

by the irradiation, showing little but emphysema. Within these involved areas a few alveoli contained edema, a few leucocytes and red blood cells. Many alveoli contained a pink-staining fibrinous material which in places was condensed at the periphery to form a fibrinous, hyaline membrane. Various stages of organization of this exudate were evident, being so massive in areas as to obliterate the alveoli. The epithelium lining some of the alveoli was swollen and had in places desquamated into the adjacent air-containing spaces. A few, fat laden macrophages were dispersed throughout. Appropriate stains revealed no bacteria. . . . No evidence of Hodgkin's tissue in the lungs was found on examination of several sections."—*Angus K. Wilson.*

ABDOMEN

ABEL, MARTIN S. A barium-gelatine mixture for x-ray examination of the digestive tract. *Radiology*, Aug., 1944, 43, 175-180.

With the usual barium-water mixture the barium tends to settle out of the suspension quickly, and when a concentrated suspension is used the organ is rendered completely opaque. And the barium-water mixtures do not adhere to the wall of the gut so that in a moment no trace of them is left. The authors have devised a barium-gelatine mixture which overcomes all these difficulties. Two level tablespoonfuls of commercial gelatine are added to about $1\frac{1}{2}$ glasses of hot water and stirred into solution; one teaspoonful each of 95 per cent ethyl alcohol and a saturated solution of bicarbonate of soda are added to this. This makes a viscous sticky medium which adheres to the wall of the intestine. It is only semi-opaque. The mucosal folds of the whole length of the esophagus are clearly shown when it is given. As the mixture is rather thin it is important to have the patient correctly angled, or the shadow of the esophagus will be superimposed on that of the heart or spine and will be hard to distinguish. For the stomach this mixture has no special advantage over acacia-barium mixtures but for the barium enema it has decided advantages. The walls of the colon are distended but not obscured by the semi-opaque medium. After evacuation the mixture is held tenaciously in the folds so that they are clearly seen.

This mixture has been used by oral administration in 100 cases at the Station Hospital at

the Mississippi Ordnance Plant at Jackson, Miss., and as a barium enema in 12 cases; on the basis of this experience it is recommended for use in the routine examination of all parts of the digestive tract.—*Audrey G. Morgan.*

MAXFIELD, J. R., JR., and McILWAIN, ALBERT
J. Diagnostic value of pneumoperitoneum.
Radiology, April, 1944, 42, 346-355.

Stewart and Stein first popularized pneumoperitoneum as a method of diagnosis in this country in 1919 but it has never been given the attention it deserves. It is valuable not only in diagnosis but also in the treatment of certain diseases. Pneumoperitoneum occurs spontaneously in 75 to 80 per cent of cases of ruptured peptic ulcer. Induced pneumoperitoneum is to be used in conjunction with and not in competition with other methods of diagnosis. The authors believe the contraindications to its use have been overemphasized. They believe there are only two real contraindications—definite insufficiency of the heart and acute infection. The technique and the apparatus used are described in detail and roentgenograms given in cases in which it has proved of value. Carbon dioxide is to be preferred to oxygen or air in most cases as it is readily absorbed and causes discomfort for only a few minutes. The roentgenograms should be taken as soon as possible after the gas is injected.

Induced pneumoperitoneum may confirm or refute clinical findings. It enables the roentgenologist to study the size, shape and position of the abdominal and pelvic viscera, to determine the presence, location, extent or absence of abdominal adhesions, to establish the location of masses in the abdomen or retroperitoneal space, to obtain information regarding the presence and extent of peritoneal implants, to determine whether a lesion is above or below the diaphragm and to identify an intrauterine or abdominal pregnancy. In radiation therapy it makes it possible to remove the intestines from the field of irradiation.—*Audrey G. Morgan.*

PALMER, WALTER L., SCHINDLER, RUDOLF, TEMPLETON, FREDERIC E., and HUMPHREYS, ELEANOR M. Syphilis of the stomach; case report. *Ann. Int. Med.*, March, 1943, 18, 393-406.

The patient was a male, thirty-six years of

age, complaining of anorexia, bloating, distention, abdominal distress, nausea, vomiting and loss of weight. He had been perfectly well until eleven months previous to admission when he began to notice a continuing loss of appetite. Occasionally nausea appeared in the mid-afternoon and usually led to emesis unless relieved by food. In the six months prior to admission the patient had lost 25 pounds in weight. Additional history was essentially irrelevant except for the statement that at the age of seventeen, following coitus with an infected person, the patient had developed a pimple on the dorsal shaft of the penis over which a crust had formed with healing in four weeks. Physical examination was essentially negative. The blood Wassermann and Kahn reactions were both strongly positive on two occasions. The spinal fluid Wassermann test was negative. The cell count was 6, Pandy negative, the pressure normal, the colloidal gold curve normal.

A gastrointestinal examination was done and the impression of the radiologist was that there was a frank ulcerative lesion in the pyloric antrum and probably also the second portion of the duodenum, nature not determined. On gastroscopic examination the gastroscopist had the following impression: (1) carcinoma, Type III, of the antrum, limited by a wall at the lesser curvature but diffusely infiltrating the posterior wall; (2) extensive atrophic gastritis; (3) Type III carcinoma usually does not give a good prognosis but in this case the upper margin is so far distant from the cardia that the attempt of a resection must be made.

A partial gastrectomy was performed. Histopathologic examination of the lesion revealed that the outstanding characteristic was accumulation of inflammatory cells, both diffuse and perivascular, scattered small follicle-like groups of round cells, and gummatoid or tuberculoid granulomata, and a large but quite superficial ulcer.

The authors state that from the point of view of gross and microscopic pathology there are no absolutely pathognomonic lesions of gastric syphilis or indeed of syphilis anywhere in the body. In most cases the diagnosis must rest on presumptive evidence. The characteristics of the gastric lesion here presented are certainly similar to those reported cases in which there is little doubt of the syphilitic etiology. It is felt that this is almost certainly

an example of ulcerative gummatous syphilis, using the term gummatous in its broadest sense as applicable to all syphilitic lesions which terminate in scarification.—*J. J. McCort.*

FELDMAN, MAURICE. Responsibility of the roentgenologist in the wartime duodenal ulcer problem. *Radiology*, April, 1944, 42, 356-358.

The selective service regulations place the responsibility for the diagnosis of duodenal ulcer on the roentgenologist. If these ulcers are not diagnosed the patient may be found to have a duodenal ulcer after induction into the service, sometimes with serious complications such as perforation or hemorrhage. Since the roentgen demonstration of a marginal deformity or ulcer crater or niche defect is pathognomonic of duodenal ulcer, it is often thought that roentgen diagnosis of this condition is easy. But it must be remembered that these are not early signs and that to prevent overlooking these ulcers it is necessary to be familiar with the early mucosal changes such as veiling of the mucosal pattern, edema and superficial induration in the ulcerated area, elevating the mucosa, obliteration of the folds over the ulcer area, thickening of the folds, distortion of the longitudinal folds, cross-bar folding of the mucosa at right angles to the long axis of the duodenal bulb, a criss-crossing, lace-like or checker-board appearance of the mucosal pattern and convergence of the folds toward the ulcer. One of the earliest signs of duodenal ulcer is fragmentation of the barium-filled bulb due to localized edema and spasm. Though it is not so pathognomonic as marginal deformity or niche, it is sufficient for diagnosis and as it occurs in the earliest stage of ulcer it is very important to be able to recognize it. It is best demonstrated on roentgenoscopic examination, using manual compression. In addition to these mucosal changes, there are physiological changes that cause secondary roentgen signs such as irritability of the bulb of the duodenum, altered motility, altered tone and spasticity.—*Audrey G. Morgan.*

REILEY, W. E. Relation of coincident anomalies of the gastro-intestinal tract and renal ptosis to digestive disturbance. *Radiology*, July, 1944, 43, 30-34.

A series of 179 patients (61 males and 118

females) with duodenal regurgitation were studied. This anomaly was found to be associated very frequently with abnormal mobility of the kidney and a short first metatarsal. Feet with short first metatarsals are weak and often associated with spastic piriformis muscles and movable kidney.

In 80 per cent of these cases with duodenal regurgitation there were digestive disturbances and in 72 per cent abnormal mobility of the kidney. The close relationship between the digestive and urinary tracts is not appreciated at its true value. Traction on the kidney pedicle causes a nervous response which results in nausea, vomiting, constipation, flatulence, nervousness and fatigue. Duodenal regurgitation is frequently a reflex from disease of the upper urinary tract and if seen it is an indication for careful examination of the urinary tract. Duodenal regurgitation, hypofunction of the gallbladder, spastic colon and movable kidney are frequently found associated and ptosis of the kidney is very common in gallbladder disease. Chronic gallbladder disease of itself does not cause nausea. If there is nausea it indicates a lesion of the upper urinary tract.

The duodenal regurgitation and other digestive disturbances associated with ptosis of the kidney may be relieved by an abdominal binder or nephropexy.—*Audrey G. Morgan.*

HEFKE, H. W. The roentgen diagnosis of hypertrophic pyloric stenosis in infants. *Radiology*, Sept., 1944, 43, 267-271.

The first symptom of hypertrophic pyloric stenosis in infants is vomiting which occurs about two to three weeks after birth. In the majority of cases it can be diagnosed clinically by palpation of the tumor but there are a certain number of cases in which roentgen examination is required for diagnosis. The most important roentgen sign is the narrowed prepyloric canal which can be demonstrated by fluoroscopy and on films. Films must be made in the right oblique position for on an antero-posterior view the pylorus and duodenal cap are often not seen.

The pyloric opening time is of importance. The normal pylorus in an infant will practically always open and discharge barium into the duodenum during the feeding. If the opening time is delayed more than five minutes pyloric stenosis is very probable. The emptying time

of the stomach is of much less importance. In many cases of proved disease with large tumors the opening time is delayed up to as long as an hour but the emptying time was normal, that is, in three to four hours no barium remained in the stomach.

Among more than 150 infants examined by the author on a suspicion of pyloric stenosis the tentative diagnosis was confirmed by roentgen examination and a Ramstedt operation performed. In 3 cases the clinical diagnosis was not confirmed by roentgen examination and no tumor was found on operation. In 38 cases the clinical diagnosis was not confirmed by roentgen examination and the later clinical course proved the roentgen diagnosis correct. After a Ramstedt operation the pyloric opening usually becomes normal in a short time.—*Audrey G. Morgan.*

HUNT, CLAUDE J. Correlation of the x-ray diagnosis with the operative findings in small-intestinal obstruction. *Radiology*, Aug., 1944, 43, 107-114.

Roentgen examination should be used much more than it is in the diagnosis of obstruction of the small intestine. In 1914 Case described gas shadows in the small intestine as an aid in the diagnosis of obstruction, and Kloiber in 1919 first stated that the diagnosis could be made from the gas shadows and a contrast medium was not necessary. But the typical transverse pattern described by Case is not necessary for the diagnosis of obstruction of the small bowel. Any collection of gas in the small intestine of an adult indicates obstruction and it develops within four or five hours of the beginning of obstruction. The distribution of the gas indicates the probable type of lesion. In mechanical obstruction by adhesive bands only the small intestine is distended while in paralytic ileus both the large and small intestine are distended. It may require a number of films to prove paralytic ileus. The painless abdomen is also a point in differential diagnosis and in fact both clinical and roentgen findings must be studied and carefully correlated. Simple mechanical obstruction may not require immediate operation but immediate operation is imperative in loop obstruction, volvulus or strangulation on account of the danger of gangrene of the intestine. Simple mechanical obstructions are probably the commonest type

and they can be diagnosed early by roentgen examination. Typical cases of the various types are described and illustrated by roentgenograms.

In early cases the use of the Miller-Abbott tube is valuable in bringing about decompression. It may be dangerous in strangulated obstruction where the viability of the intestine is in danger. Intubation should be carried out by the roentgen department as it can be done successfully only under fluoroscopic control. The technique of intubation is described in detail.

The barium enema is valuable in the reduction of intussusception.—*Audrey G. Morgan.*

VIAMONTE, J. MANUEL, and FARINAS, PEDRO L. Diagnóstico radiológico de la amebiasis cólica. (Roentgen diagnosis of amebiasis of the colon.) *Vida nueva*, Jan., 1943, 51, 1-19.

Amebiasis is endemic in tropical countries and its diagnosis is very important. The clinical picture is characteristic in the late stages but it is important to diagnose it in the early stages when treatment is effective and the clinical picture at this stage may be confused with that of many other diseases. Roentgen diagnosis therefore becomes extremely valuable and is possible even at an early stage. The different stages of the disease are described and illustrated with drawings and roentgenograms of clinical cases.

Speder, working in French Morocco, classified the disease into six stages, the atonic, accordeon, rough cord, irregular, in which the contrast medium is distributed irregularly over the surface of the colon, rigid and filiform. These names are descriptive. To these the authors add those of diffuse and localized amebic tumor. These tumors may very readily be confused with the tumors of tuberculosis or syphilis. Examination may be made by a contrast meal or contrast enema, preferably both. Such examinations show the extent and the stage of the lesions.

Histopathological examination for amebae is not sufficient for it is positive in only about 20 per cent of the cases. Negative rectosigmoidoscopy does not disprove the disease as there are not always lesions of the rectum or sigmoid. It is hoped that this article will stimulate commoner use of roentgen examination in this disease.—*Audrey G. Morgan.*

MACHT, STANLEY H. Foreign body (bottle) in the rectum. *Radiology*, May, 1944, 42, 500-501.

A case of foreign body in the rectum is described as a medical curiosity. The patient, a sailor thirty-one years of age, entered hospital complaining of pain in the lower abdomen, inability to defecate and bleeding from the bowel on attempted defecation. The day before he had drunk himself into an alcoholic coma. Roentgen examination showed a bottle, with its open end upward, in the sigmoid and iliac colon. Under spinal anesthesia it was extracted manually; in a week pain and tenderness had disappeared and the patient was discharged.

A number of other cases of curious foreign bodies in the rectum are reviewed from the literature. This is the eighth case in which a bottle in the rectum has been reported.—*Audrey G. Morgan.*

FAUST, DANIEL B., and MUDGETT, CHARLES S. Visualization of the biliary tract with air and barium following a barium meal. *Ann. Int. Med.*, August, 1943, 19, 356-367.

An excellent review of all the pertinent literature up to the present time is given. It was noted in the cases reviewed that the appearance of air in the gallbladder was due either to a gas bacillus infection of the gallbladder, or to a fistulous communication from the biliary tract to the stomach, the duodenum, or the colon, either spontaneous or surgical in origin. Numerous instances were recorded in which the biliary tract, in part or as a whole, has been outlined with barium following a barium meal or a barium enema but without air being noted in the biliary tract. In these cases spontaneous or surgical fistula were present in the great majority. In many instances there had apparently been a direct passage of a calculus from the gallbladder to the duodenum, either the duodenal bulb or the second portion of the duodenum, or to the colon—most commonly the hepatic flexure. Seventeen cases have been reported in which no fistula was demonstrated and in which the biliary tract was outlined with barium to a greater or less extent. In none of these cases without fistula was there any air noted in the gallbladder or common duct. It is believed in these cases that the barium gained entrance into the biliary tract through an incompetent sphincter of Oddi and perhaps this incompetency accounted for the symptoms in these cases.

In cases without fistula, as in those with fistula, the symptoms vary but in most instances were referred to the upper abdomen. A variety of conditions was noted in the cases with incompetency of the sphincter of Oddi, the most frequent being duodenal ulcer and tumors in the upper abdomen. No definite conclusions could be drawn from this small group of cases.

The authors were not able to explain in the case they reported the finding of air in the biliary tract by either a gas bacillus infection of the gallbladder or a fistula between the biliary and gastrointestinal tracts. There was undoubtedly relaxation of the sphincter of Oddi with general atony of the biliary tract. No case has been found in the literature in which the biliary tract has been visualized and air seen in the gallbladder without a fistula being present, as was in the case reported here. An exploratory laparotomy had been done on the patient. The stomach was found to be normal. The duodenum was opened and explored for a distance of 8 inches and no polyp, tumor, or ulcer was found. The gallbladder was adherent to the second portion of the duodenum and was easily freed. Traction from the cholecystoduodenal adhesions may have played a part in producing the incompetency of the sphincter of Oddi. Releasing the adhesions at operation followed by the use of a bland diet, low in fat, afforded this patient symptomatic relief.—*J. J. McCort.*

BAYLIN, GEORGE J., and WEEKS, KENNETH D. Some roentgen aspects of pancreatic necrosis. *Radiology*, May, 1944, 42, 466-470.

A case of pancreatic necrosis in a white cotton-mill worker forty-two years of age is described. He was admitted to the hospital with clinical signs that suggested obstruction of the large bowel and portal obstruction possibly due to cirrhosis of the liver. A plain roentgenogram of the abdomen showed a mottled appearance due to irregular rounded areas of increased density. They showed no calcification. A roentgenogram with a stomach tube in place showed the tube deflected to the right and upward. A study after giving a barium enema showed areas of spasm associated with loss of normal mucosal detail. These were in the mid-transverse colon, the splenic flexure and the ileocecal region. The mottling was attributed to fat necrosis and subsequent saponification resulting from pan-

creatitis. The displacement of the stomach to the right and upward was thought to be due either to swelling of the pancreas or to sealing-off of the foramen of Winslow with resultant accumulation of fluid in the lesser omental bursa. The intestinal spasm was thought to be due to the fat necrosis and the peri-intestinal inflammation caused by it. Operation confirmed the diagnosis of necrosis of the pancreas. The patient died and the autopsy findings are described in detail.

In this case the bases of the lungs were not roentgenographed, though basal exudates often occur in necrosis of the pancreas. The "inverted figure 3 sign" has been considered of great importance in changes in the head of the pancreas. The authors found it only once in the careful study of several cases of carcinoma of the pancreas. But on the basis of this sign plus spasm of the duodenum they made a diagnosis of pancreatitis which was confirmed by operation.—*Audrey G. Morgan.*

GENITOURINARY SYSTEM

OSGOOD, ELLIS C. Value of the delayed examination in pyelography. *Radiology*, April, 1944, 42, 380-381.

Sometimes, as in hydronephrotic kidney for example, diagnosis can be made from roentgenograms taken as long as twenty-four hours after retrograde pyelography when it could not be made from films taken immediately afterward. An illustrative case is described in a woman of eighty-one who came for examination on account of right lower quadrant pain irradiating to the back. Roentgen examination showed a large soft tissue mass in the right kidney area. A retrograde study on the right showed a circular dye shadow with poorly defined margins in the kidney region. A roentgenogram made twenty-four hours later showed that the dye had diffused throughout the soft tissue mass, showing that it was a large hydro-nephrotic sac.

To determine whether such late films should be made the routine films should be studied at once; the appearance of these films will also show the time that should elapse before the delayed examination is made.—*Audrey G. Morgan.*

HOWES, WILLIAM E. Kidney tumors; classification, review of symptoms. methods of diag-

nosis, therapy, and end-results. *Radiology*, April, 1944, 42, 319-328.

Tumors of the kidney are difficult of diagnosis because they have generally grown to large size and often metastasized before they are discovered. Tumors of the cortex may not cause hematuria until they break into the pelvis and are not apt to cause pain until they invade the capsule; the patients seldom notice the mass themselves, at least until it is very large.

The Brooklyn Cancer Institute uses the following classification of kidney tumors: (1) tumors of the kidney cortex (*a*) papillary adenocarcinoma; (*b*) alveolar adenocarcinoma; (*c*) adenomyosarcoma (Wilms' tumor); (2) tumors originating in adrenal rests; hypernephroma; (3) tumors originating in the kidney pelvis: (*a*) papillary epithelioma; (*b*) alveolar carcinoma. Grawitz' theory that hypernephromas originate from adrenal rests in the kidney is now doubted. A large proportion of cases reported as hypernephroma are really renal adenocarcinoma. Primary kidney tumors may be radiosensitive but metastases, especially to bone, are radioresistant.

The author reports 59 cases of malignant tumor of the kidney seen at the Brooklyn Cancer Institute among a total of 6,400 admissions, or 0.65 per cent of admissions. Of these 45 were proved by autopsy or nephrectomy while 9 were not confirmed pathologically. Pain was the outstanding and first symptom in 29 cases, hematuria in 21; in 4 the first sign was the abdominal tumor. Only 11 of the patients are still living and only 5 of these are free of metastases for over three years. The author has seen a recurrence of tumor twenty years after nephrectomy. Nephrectomy was performed in 38 of these cases and but 5 of these have survived over three years without known metastases. All of these surviving patients were given postoperative roentgen treatment and one was given large amounts of preoperative irradiation.

Unexplained back pain and loss of weight and strength should be considered indications for careful examination for kidney tumor and transitory hematuria should never be disregarded. Diagnosis is made by roentgen examination and clinical and laboratory findings. Bone metastases must not be confused with primary bone tumors. A further study should be made of the value of preoperative roentgen

irradiation. Histories and roentgenograms of noteworthy cases are given, and a tabulation of the end-results.—*Audrey G. Morgan.*

BIXLER, LOUIS C., STENSTROM, K. WILHELM, and CREEVY, C. D. Malignant tumors of the kidney: review of 117 cases. *Radiology*, April, 1944, 42, 329-345.

The history of tumors of the kidney is reviewed and 117 cases seen at the University of Minnesota Hospital from 1924 to 1940 discussed. These were followed up to the end of 1942. They included 94 cases of carcinoma of the renal cortex, 13 cases of Wilms' tumor, 9 of carcinoma of the renal pelvis and 1 of sarcoma. Tables showing the symptoms, treatment and results are given.

The average age of the patients was 53.4 years and 63 per cent were males and 37 per cent females. The chief symptoms were hematuria, pain, abdominal mass, loss of weight and weakness. Even the slightest hematuria should be considered an indication for thorough examination, including urography.

Metastases were demonstrated at the time of diagnosis in 14 of the 81 proved cases of carcinoma of the cortex. There is some question as to the advisability of nephrectomy if there are metastases at the time of diagnosis. The authors conclude that nephrectomy is not contraindicated by one small metastatic lesion in the lung or in bone. They believe that irradiation of metastases and recurrences is definitely worth while. Even if it does not prolong life it relieves pain and makes a fairly normal life possible for the patient. It seems to be generally agreed that irradiation alone does not cure carcinoma of the cortex. The value of postoperative irradiation is not established. The authors think it is worth while in some cases as it delays the growth of any cancer cells that may possibly remain.

Nephrectomy is the treatment of choice for malignant tumors of the kidney except Wilms' tumor. In Wilms' tumor irradiation seems to be of greater value than in any other form of malignant kidney tumor. The treatment in these cases consisted of surgery alone in 17 cases, surgery plus irradiation alone in 18 and irradiation alone in 13. Only cases proved histologically are considered in the results. The details of the roentgen technique used are discussed.

In adenocarcinoma of the cortex the five year survival rate for cases treated by surgery alone was 50 per cent, for cases by surgery plus irradiation 31 per cent, by surgery plus immediate postoperative irradiation 42 per cent and by irradiation alone 8 per cent. There were no five year survivals among the Wilms' tumor group, but 3 of the patients are still living and well with no signs of metastasis, 1 after four years and eight months. The survival rate in carcinoma of the pelvis is 16 per cent and for the whole series of kidney tumors 27 per cent.—*Audrey G. Morgan.*

MISCELLANEOUS

WILSON, C. W. Some condenser ionization chambers for the measurement of x-ray dose. *Brit. J. Radiol.*, March, 1944, 17, 86-89.

Commercial dosimeters can be used for the ordinary measurement of the output of roentgen tubes, but for more specialized work suitable ionization chambers must be made in the laboratory workshop. The Victoreen dosimeter which makes use of the condenser chamber principle is the one usually preferred for the calibration of tubes; small condenser ionization chambers using the same principle may be used in conjunction with a suitable electrometer for most other types of investigation.

Two types of chamber are described and illustrated with diagrams. They are condenser ionization chambers with the Wulf bifilar electrometer. Their simplicity and usefulness is increased by the use of an air-wall material which is a bakelite-graphite mixture containing a small percentage of vanadium pentoxide; it can be moulded under heat and pressure. The first type is intended for routine calibration measurements of tube output. A small cylindrical ionization chamber is mounted at the end of a stem, in a manner similar to that of the Victoreen chamber. The second is intended for more experimental work, such as the determination of the volume distribution of radiation by means of direct measurements on patients. In this type the ionization chamber constitutes the whole apparatus, the maximum overall dimension being not more than 1 cm.

The behavior and response of the chambers when irradiated is described and graphs given showing the effect of wall thickness on the measurement of roentgen rays over a range of wavelengths.—*Audrey G. Morgan.*

BRAESTRUP, CARL B. Depth dose measurements for 100-, 120-, and 135-kv. roentgen rays. *Radiology*, March, 1944, 42, 258-272.

As larger doses are being used in the treatment of superficial cancer it becomes increasingly important to know the amount of radiation given to the underlying healthy tissue. This information has been limited by the lack of complete depth dose tables for low and intermediate voltages. This article is largely made up of tables showing phantom measurements of depth doses for half-value layers from 1.0 to 8.0 mm. aluminum (0.04 to 0.44 mm. copper). The equipment and measuring instruments are described and the comparative value of phantom materials discussed. Masonite presdwood should not be used for radiations produced at less than 200 kv. even if its density is unity. Water simulates human tissue much more nearly and its availability in a pure state permits of better duplication of results between different laboratories. The values obtained with presdwood are in general higher than those for water, especially at the greater depths.

The wide range of depth doses obtained with the four ray qualities used in this study indicates that low and intermediate voltage therapy could be carried out more effectively with a limited number of techniques. This would permit of better correlation between clinical results and physical factors. Half-value layers of 1.0, 2.0, 4.0 and 8.0 mm. aluminum as used here should be sufficient for most clinical purposes. And two target-skin distances, 15 cm. for small fields (5 cm. or less in diameter) and 30 cm. for large fields should be sufficient for the majority of superficial lesions.—*Audrey G. Morgan.*

MAYNEORD, W. V., and CLARKSON, J. R. Energy absorption. II. Integral dose when whole body is irradiated. *Brit. J. Radiol.*, June, 1944, 17, 177-182.

This paper discusses an experimental study of the absorption of energy during roentgen and radium treatment, particularly when the whole body is irradiated. The unit of integral dose suggested is the gram-roentgen—that is, the energy conversion when 1 roentgen is delivered to 1 gram of air. For clinical purposes 1 megagram roentgen, that is, 1 million gram roentgens is used.

A model of a patient was constructed that had elliptic cross-sections at all levels; it was

made of paraffin wax and slabs of mixed rice flour and sodium bicarbonate. In measuring energy absorption in the model, condenser chambers were placed at the centers of mass of equal "cells" of a given section. The integral dose was obtained in three ways: (1) from the mean of the indications of the chambers (average dose method); (2) by drawing complete dose distributions in a given plane, followed by planimetry of the areas between dose contours, and (3) making use of the fact that under certain conditions the dose at the center of gravity of a cross-section is equal to the average dose in that section.

A very wide range of experimental irradiations was used, covering half-value layers from 0.037 mm. copper (40 kv.) up to 10 mm. copper (gamma rays of radium). Tables of the integral doses obtained in this way are given.

The average dose per roentgen on the skin for a patient of normal size varies from approximately 0.8 r for gamma rays to 0.175 r for low voltage irradiations. It is found that the integral dose per surface roentgen varies with quality in a complex way which may be predicted theoretically, the main practical result being that for half-value layers below approximately 1 mm. copper the integral dose falls very rapidly with decreasing half-value layer.

The relative integral doses in wax and in powder mixture were studied. The variation of the integral dose with changes in the direction of the roentgen-ray beam was also studied. The values for external radium sources were found by making use of reciprocity relationships between source and irradiated object.

The integral doses with smaller focal-skin distance roentgen techniques were measured in a few cases to provide data for those who use irradiation of the whole body with small doses. The importance of integral dose in problems of protection is pointed out, particularly with regard to the great variation of integral dose per surface roentgen with changes in half-value layer.

The measurements show the fallacy of considering 50 r in a whole body irradiation as a "small dose," for when applied in this way the integral dose may reach 3 megagram roentgens, an amount comparable with that absorbed during the whole of a severe localized treatment.

There is a marked increase of integral dosage rate on approaching powerful radium sources.

The study of integral dose will frequently show relationships that are not brought out by a study of dose alone.—*Audrey G. Morgan.*

WOLF, BERNARD S. Nomographic aids in calculating radium dosage for plane and point sources. *Radiology*, April, 1944, 42, 368-374.

Calculations of radium dosage were simplified by the contributions of Paterson and Parker published in the *British Journal of Radiology*. For radium sources filtered by 0.5 mm. platinum or its equivalent, distributed on square or circular areas, the number of milligram-hours required to deliver 1,000 gamma roentgens could be determined from a group of graphs. The same data can be put in the form of an alignment chart or nomogram. Such a nomogram is illustrated. It consists of three vertical scales. The area in square centimeters is given on the left-hand scale. The treatment distance in centimeters is given on the center scale. The right hand scale has divisions on both sides. The divisions on the right side of this scale are labeled at the top mg-hr. and the divisions on the left side are labeled %.

The method of using the nomogram is described and illustrated by examples and correction figures given for filtrations other than those equivalent to 0.5 mm. platinum and for tissue absorption if the source of radiation is surrounded by tissue. These data are based on the assumption that the source of radiation is a point, which of course it never is in actual practice. The calculated dose is therefore a little too high, but in the average case the error

is not more than 5 per cent.—*Audrey G. Morgan.*

JONES, D. E. A. Dosage system for linear gamma-ray sources. *Brit. J. Radiol.*, Feb., 1944, 17, 46-47.

In cases requiring radium treatment of an approximately cylindrical surface, such as the rectum, vagina or uterus, a linear radium source is generally used, contained in some form of tubular applicator. The dose is calculated at the middle point of the linear source. But this gives the maximum dose, as the dosage decreases towards the ends of the linear source. Where greater uniformity is necessary the axial source may be divided into three parts, the middle one of which is weaker than the two end ones. Calculations of the actual dosage rates are based on Sievert's formula for a linear source contained in an absorbing cylinder. The necessary formulas are given and also two graphs showing the results which have been confirmed by experimental work at the Lambeth hospital for over two years using rectal applicators of the Tod type and vaginal colpostats. One of these graphs gives the percentage content of the central source and the other gives the milligram-hours required for a dose of 1,000 r for different shapes of applicator. If a considerable amount of a particular type of treatment is given in a hospital, such, for example, as carcinoma of the uterus, it is well to have sets of tubes made up of the size and content required for standard cases. In other cases supplementary radon sources may be used.—*Audrey G. Morgan.*



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RESULTS OF ROENTGEN TREATMENT OF LEUKEMIA*

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THE value of roentgen treatment in chronic leukemias is generally acknowledged as an excellent palliative measure. There is optimism and pessimism in the varied reports of results, especially in the statistical appraisals of a possible increase in the longevity cycle.

It was for this purpose that a review of the records of all cases of chronic myelogenous and lymphogenous leukemia at the Philadelphia General Hospital was undertaken five years ago. The findings at that time were considered disappointing. The history records and pertinent laboratory data were interpreted as being confusing, and the report was accordingly set aside. Since that time additional patients and further changes of technique have been observed. The problem and the interpretation of results were considered from another point of view. All pertinent factors in the clinical status were evaluated. Special attention was directed to an estimation of the life span in relation to the many varied technical factors employed.

It was hoped that there might be strong evidence to support a conclusion of the possible decided superiority of a particular irradiation technique. The advantages or disadvantages of fractionated small or large doses confined to the spleen or enlarged

lymph nodes, or generalized irradiation of the entire body—so-called teleroentgen or “spray” techniques—were meticulously tabulated according to the final results. The correlation and evaluation of such information was essentially the objective and special scope of this analysis, and a brief summary and interpretation of the evidence is herewith submitted.

A review at this time of the records of 110 patients shows very interesting and concrete data which might reasonably be considered a representative cross section of the actual results and experiences in the radiation management and treatment of chronic leukemia. This evaluation includes all cases, even the very advanced, in which no significant irradiation could be given. Practically all the cases in the series were relatively comparable. Their illness was sufficiently severe to require hospitalization. The ratio of age, sex and race showed no significant deviation from that noted in other reports in the literature.

The symptoms were strikingly insidious. They were predominantly weakness, loss of weight, cough, dyspnea, edema of extremities, abdominal pain and fullness. Enlargement of the spleen and lymph nodes varied in degree but was usually marked and generalized.

* From the Department of Radiology of the Philadelphia General Hospital. Read at the Joint Meeting of the American Roentgen Ray Society and the Radiological Society of North America, Chicago, Ill., Sept. 24-29, 1944.

Biopsies of bone marrow (sternal) and lymph nodes were done in 21 per cent of the cases.

Of the 110 patients, 46 were too ill to undergo treatment (Table I). They were

TABLE I

	Number of Cases		
	Lym- phoid	Myeloid	Total
Too advanced for irradiation	25	21	46
Irradiation: no "follow-up"	9	6	15
Irradiation: Adequate "follow-up"	24	25	49
	58	52	110

practically moribund when admitted to the hospital. Two of these cases were clinically acute myeloid and 2 cases were acute myeloid-leukemic types. None lived longer than one month. It is interesting to note

that almost all of these patients had been ill less than six months before hospitalization. In 7 cases the duration of symptoms was less than two weeks, yet the subsequent clinical course showed them to be chronic cases. In 6 instances the symptoms had been present longer than one year.

Of the patients to whom irradiation was administered, 15 could not be traced after discharge from the hospital. This group obviously cannot be considered for any statistical purpose.

The present study is limited to 49 patients who were followed throughout their illness. Of these, 28 died, and 21 are still under active treatment (Chart 1). Twelve patients (50 per cent) lived six months or less; 17, or 70 per cent, lived three years or more; 7 lived more than five years. Two patients lived thirteen years, 1 eighteen years and 1 nineteen years. This is a good summary of the status of the controlled irradiated patients in relation to the life span from the time of diagnosis and the

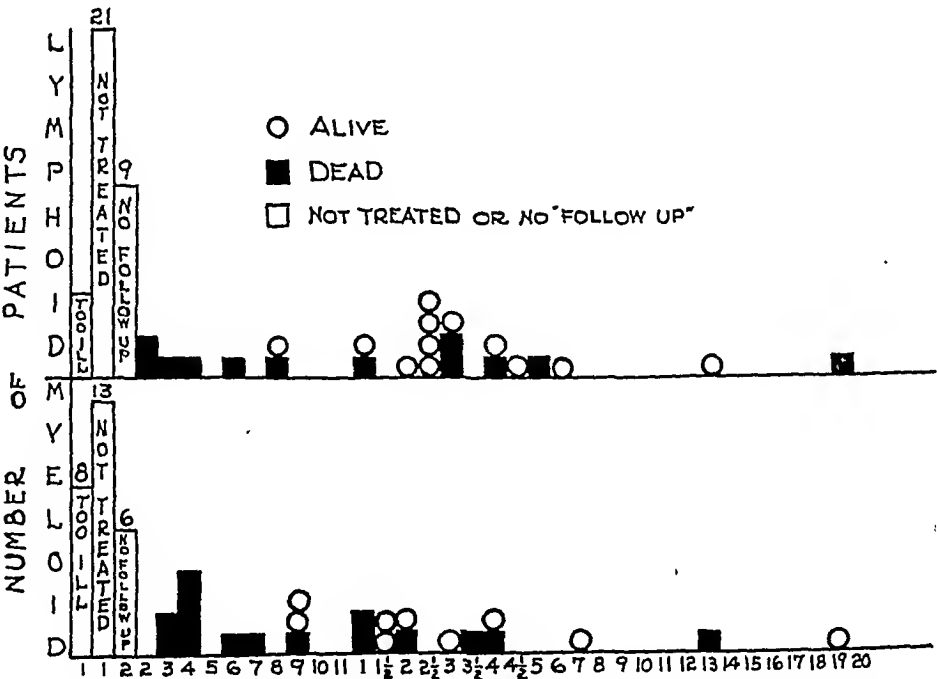


CHART 1. The life span from the time of instituting treatment is shown. About 40 per cent of the patients were too ill for irradiation when admitted to the hospital. Of the irradiated patients 13 per cent could not be traced. The life span after instituting treatment was 39.7 months for the lymphoid, and 32.2 months for the myeloid leukemias.

beginning of treatment. There was practically no appreciable difference in the clinical course or the life span of the lymphoid and myeloid types.

It might be argued that the ones who died within six months were too advanced in their disease when treatment was started. Obviously not all of the patients could be identical in extent of clinical involvement except insofar as they required hospitalization.

ment was 39.7 months (3.3 years), in the myelogenous group 32.2 months (2.7 years). One could easily add a year or more to these results if the life cycle were to be estimated from the patients' statements as to the onset of the disease. But such a method of estimating the life span for a large group would lead to erroneous conclusions, and it would undoubtedly be misleading to accept the results of such calculations.

There were 2 patients in each group

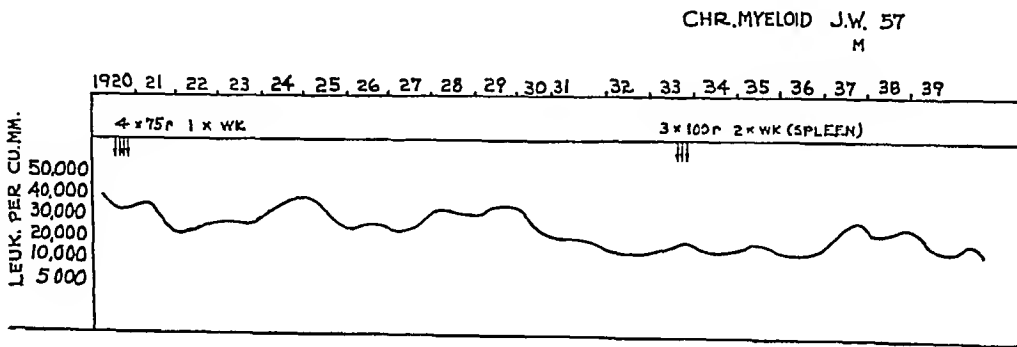


CHART II

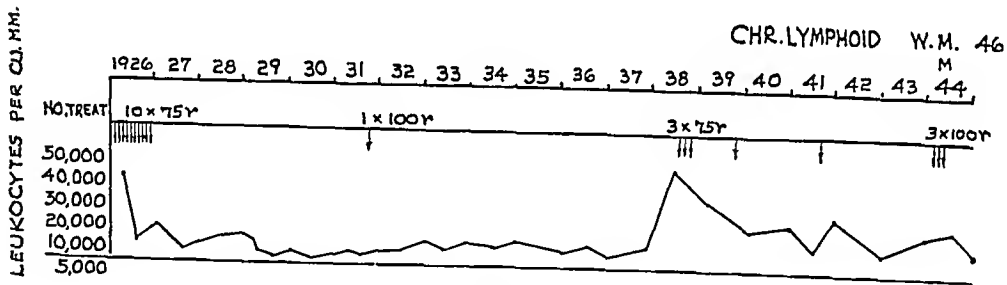


CHART III

CHARTS II and III. Long life spans and excellent clinical courses may be due to a benign character of the disease rather than to the effect of irradiation. Small fragmentary doses may have been contributory.

The difference in results must therefore be attributed to some inherent difference in the origin, character and extent of the disease, as well as to age and various complications. The factors of sensitivity and resistance to irradiation are variable.

If one were to evaluate the results of irradiation on the basis of duration of life in this group of 49 patients, the good effects would be undoubted and striking. In the lymphogenous group, the average duration of life from the time of instituting treat-

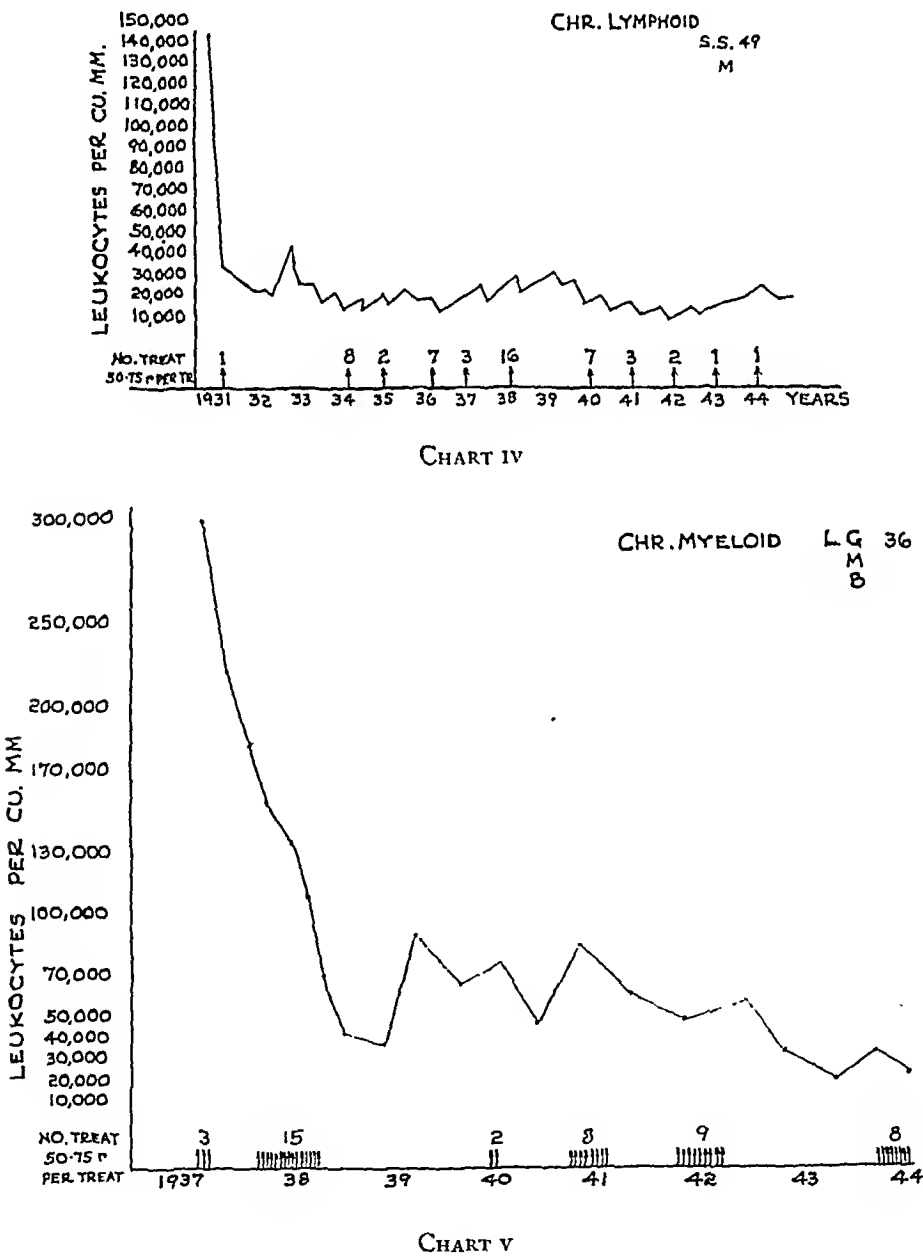
(Chart I) with life spans extending to thirteen and eighteen years in the lymphoid, and thirteen and nineteen years in the myeloid group. Unless one could show a consistent uniformity of long life for a large number of patients, it would be incorrect, for statistical purposes, to accept a mathematical determination of results in terms of life span, but rather a conclusion of value based on clinical observations.

The 4 instances in this series of an unusually long life may be the effect of a very

benign character of the disease and not attributable directly to irradiation (Charts II and III).

These results show that 30 per cent of all patients irradiated may live three years or more. About 40 per cent will be too ill to tolerate enough treatment to be of benefit. Of the treated cases, more than 50 per cent will show clinical improvement which may be of a very dramatic degree. Actual prolongation of life, which is undoubted in some patients but questionable or indeter-

minate in others, cannot be mathematically established for statistical purposes. According to Minot, Buckman and Isaacs¹ (1924), the average duration of life of 78 irradiated patients with chronic myelogenous leukemia was 3.5 years after detection of the first symptoms, as compared with three years for the non-irradiated patients. Minot and Isaacs² did not believe irradiation prolonged life in cases of chronic lymphatic leukemia. Hoffman and Craver³ reported the aver-



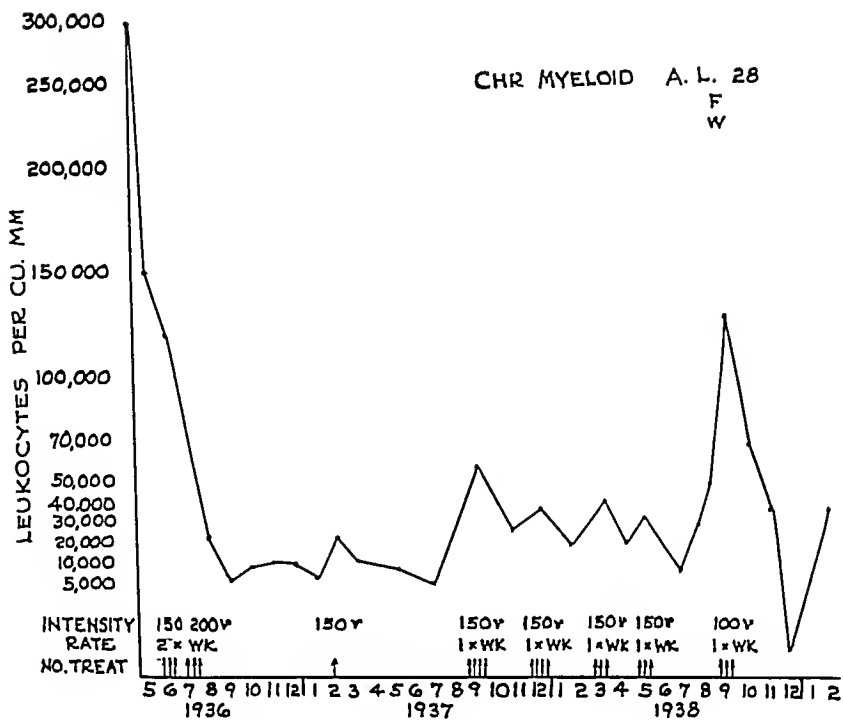


CHART VI

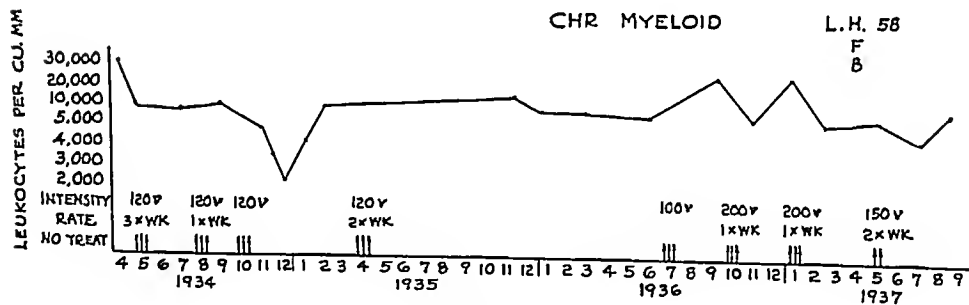


CHART VII

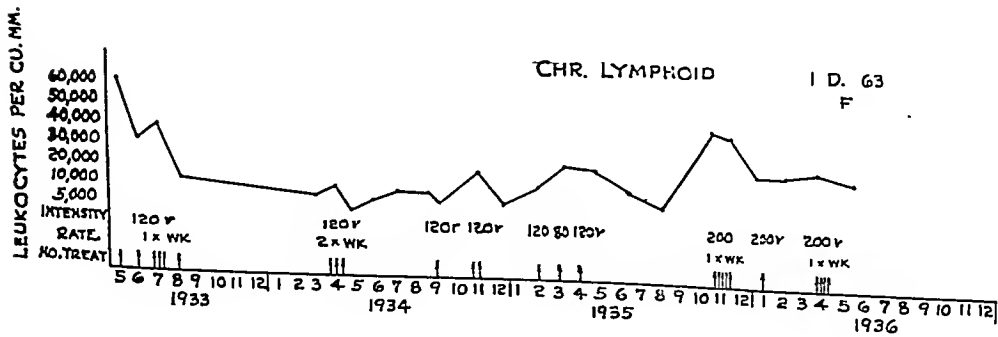


CHART VIII

CHARTS IV, V, VI, VII and VIII. Typical course of the leukocyte count with a manifold variety of small and large doses given at long, irregular intervals.

age duration of life after beginning treatment was 2.62 years for 82 patients with chronic myelogenous leukemia. They comment that "irradiation treatment causes an average increase of about ten months in the duration of efficient life as well as a period of efficiency and usefulness that the patient otherwise could not hope to enjoy."

The diverse clinical, pathological and technical factors make it very difficult to estimate for statistical purposes the life cycle of these patients from the onset of symptoms. No matter how painstakingly the histories may have been recorded, the first symptom as reported by the patient is not always reliable evidence of the onset of the disease. In many individuals the diagnosis has been made accidentally in routine blood studies. In this review, one patient was being prepared for tonsillectomy and another was admitted with pneumonia when the diagnosis of leukemia was made.

The history record of the first symptom and the time of onset may have no relation to leukemia. In this report, this information was not clearly or definitely recorded, and in many of the history charts the evidence was vague or contradictory. The occasional record of symptoms of long duration (three or more years) could easily raise the averages of the life span and the conclusions would therefore be misleading.

Each patient is an individual involving special details in treatment and in interpretation of the results. Patients with very mild or so-called benign types of leukemia may carry on for years with little or no irradiation. Patients with the fulminating or so-called malignant types, with very marked lymph node or splenic enlargement and rapidly failing health and strength, usually show progressive involvement unless treatment is instituted.

The blood count is a reliable criterion of the progress of the disease. Treatment should be withheld until the patient's symptoms require alleviation. In this series, many patients maintained an excellent status of well being and apparent good health with leukocyte counts ranging from

50,000 to 100,000. Under these circumstances, no irradiation was given unless there was evidence of general indisposition, pain (predominantly in the region of the spine or joints), or marked lymph node or splenic enlargement.

In many instances it is necessary to continue roentgen treatment until the leukocyte count reaches 40,000 or 50,000. There may be some risk in aiming to maintain a normal leukocyte level. A progressive reduction to a dangerously low level may occur even after treatment has been discontinued.

Many individuals show a marked tolerance for a very high leukocyte count and, conversely, many will manifest alarming symptoms with a relatively low, almost normal blood picture.

The use of the basal metabolic rate to indicate and to support the clinical manifestations of relapses is very excellent, as recently observed by Uhlmann and Goldner⁴ and previously described by others.^{5,6} It was employed in a small number of cases in this series. The high rate was not always commensurate with the sense of well being. It probably indicates distinct evidence of activity and is possibly a criterion for the need of irradiation despite the blood findings, which do not always reflect the actual condition of the patient. This evidence of a relapse or renewed activity is usually manifested readily and sometimes unmistakably in the general clinical course and well being of the patient.

The complexities of repeated relapses during the period of observation and treatment vary in frequency and intensity, and occur regardless of the technical procedures employed. In Murphy's⁷ series of cases this problem seemed to be controlled when he employed the "spray" technique as against a kind of intermittent massive dose technique. There was also an improvement in the life span of patients so treated. Murphy regulates the frequency of treatments according to the blood picture, which he aims to keep below the level of 30,000 to 40,000. In this series the number of patients

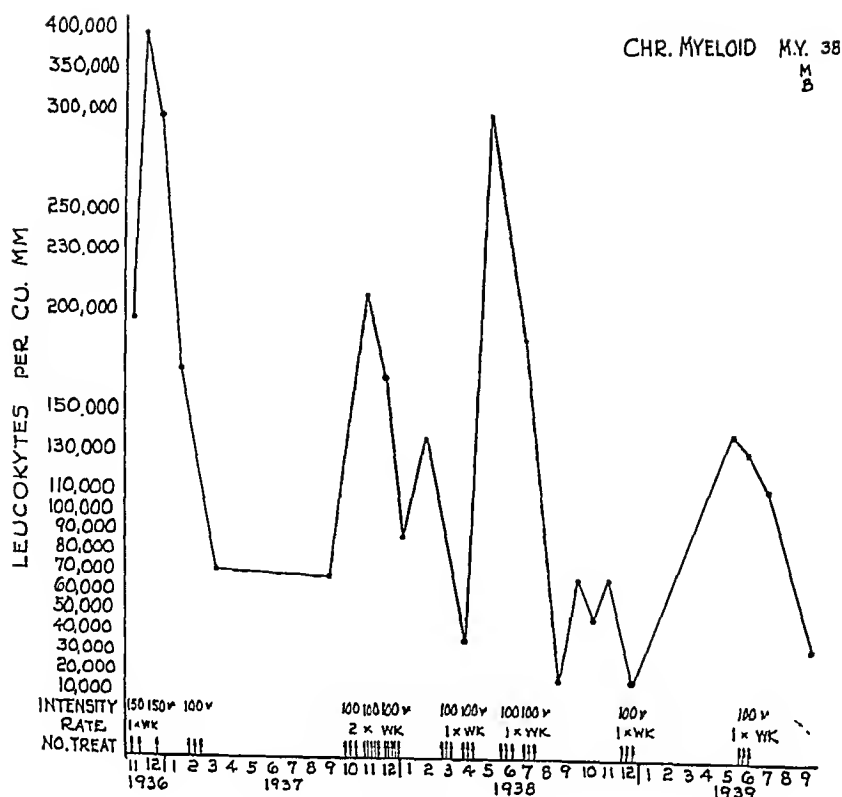


CHART IX

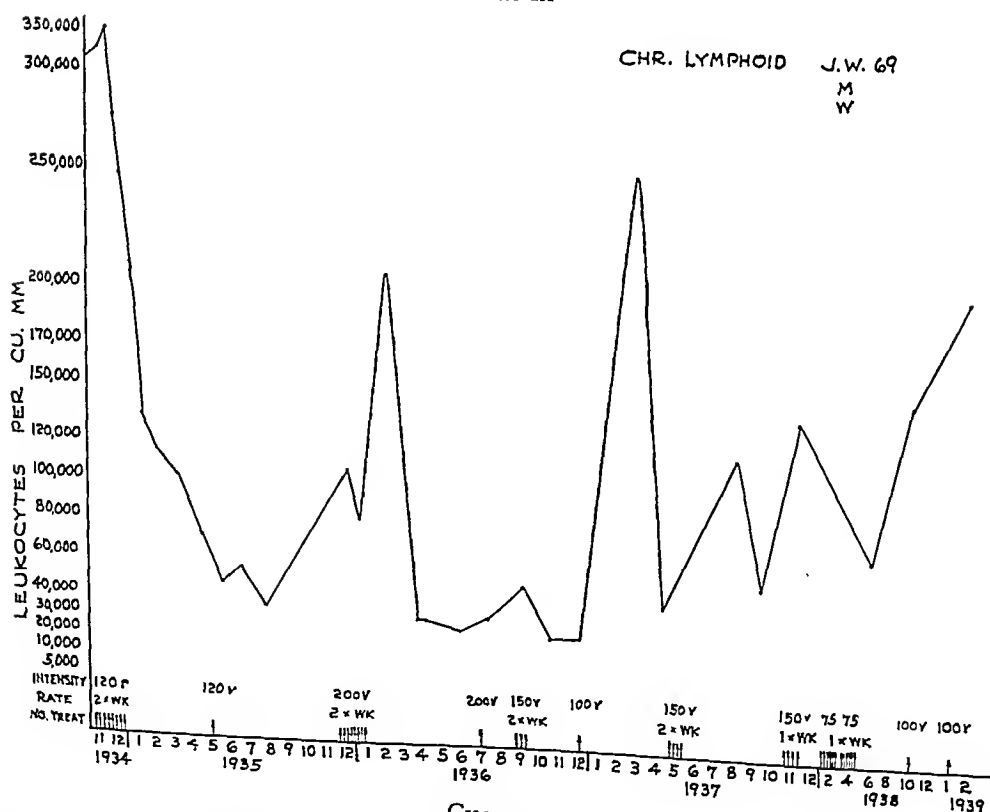


CHART X

CHARTS IX and X. Excellent clinical course even though the leukocyte count is high and relapses frequent. Note the long intervals between the treatments. Illustrates the variability of technique and leukocyte course in many favorable cases in this series.

treated with a teleroentgen technique was small. The results were not essentially different from those obtained with other localized, fractionated small and large doses.

In reviewing the literature one is impressed with the many variations of technique with reference to intensity, rate of delivery, size of field, and region treated. Excellent results, with life spans of four and five years and sometimes longer, have

and x) as was noted in groups purposely maintained at levels of 50,000 and 25,000 (Charts VII, VIII, XI, XII and XIII).

On the other hand, there were astounding variations in the clinical course, with and without treatment. Just as many patients may react well or poorly with different technical procedures of irradiation, a certain group will carry on without any kind of treatment.

There was no uniformly satisfactory technique. One should adhere to the principle of finding the smallest dose compatible with establishing a state of improvement in health and well being and efficiency. Usually 50 r (measured in air) is a safe starting basis. This may need to be given one, two, three, four or five times a week. In some cases this dose may be satisfactory if given only once or twice a month. A dose of 50 r may be sufficient at intervals of several months. The general health may be excellent for six months or a year without treatment. A satisfactory clinical status may often be maintained with these various small intensities and rates with leukocyte counts of 75,000 to 100,000, while in other groups the same clinical status is achieved only by reducing the white count to 50,000, 25,000 and 10,000 levels. This observation indicates that the rate and intensity of irradiation should be modified according to the clinical course rather than according to the leukocyte level.

been shown with a manifold variety of techniques. As in this series, no standard procedure of daily or total dose was uniformly satisfactory (Charts III, IV, V, VI, VII and VIII).

A high level in the leukocyte count may be reduced rapidly to levels of 8,000 to 10,000 and consistently maintained with a commensurate well being of the patient (Charts VI, XI, and XIV). Such a vigorous, intensive procedure in as many more patients would result in disaster—shock, collapse and shortened life. In this series of cases, the clinical course of a large group of patients was as satisfactory with leukocyte counts approximating 100,000 (Charts IX

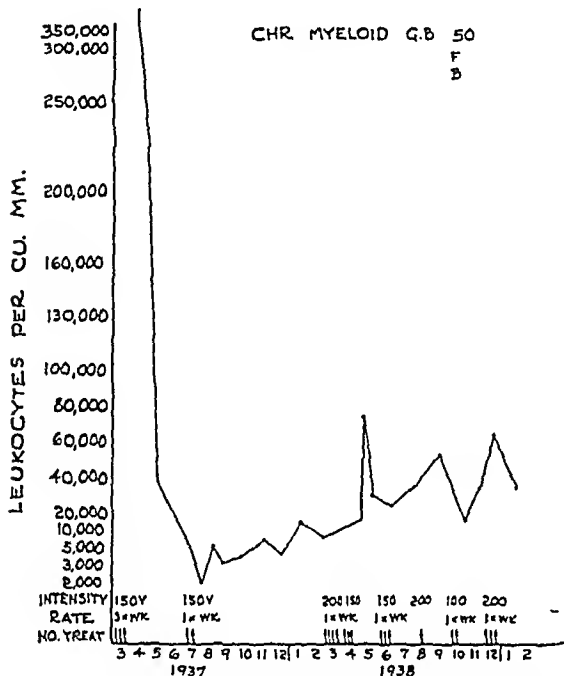


CHART XI. Favorable course with no treatment for one year, also illustrated in Charts V, VII and XIV.

There are instances when greater intensities are necessary—as much as 100, 150 and 200 r. Sensitivity to the effects of roentgen rays diminishes at variable rates (Chart VI). A patient may become refractory to the effects of small doses within six months to a year, and doses up to 200 r are necessary to bring about a stabilizing effect. In addition to regulating the dose according to the well being, one must frequently also consider additional treatment for excessive enlargement of lymph nodes or spleen.

Identical results may be obtained with 125 kv. and filtrations of 2 to 6 mm. of aluminum, and 200 kv. and filtrations of 0.25, 0.50, 1 and 2 mm. of copper. The

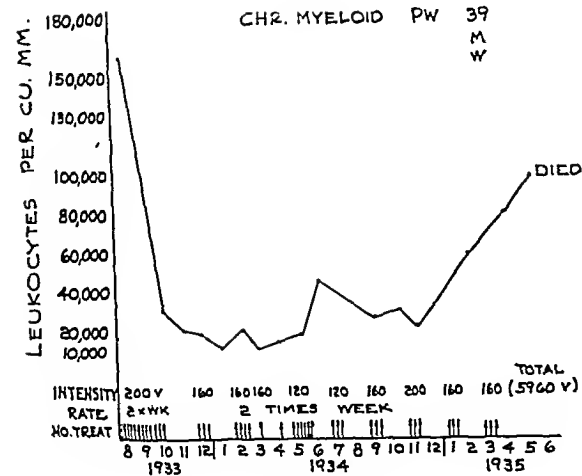


CHART XII

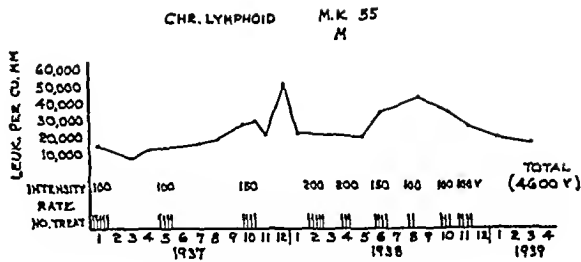


CHART XIII

CHARTS XII and XIII. Satisfactory clinical results accomplished with large daily and total doses and a rate of frequency that might be disastrous as a routine procedure. In an average case this would be excessive treatment.

majority of the patients were treated using fields of 15 by 15 cm. and 20 by 20 cm. over the spleen, mediastinum and ribs or over actual enlarged lymph node regions.

The long bones were never specially treated except when the teleroentgen or "spray" technique was employed. A single dose of 25 r for general body irradiation was used,

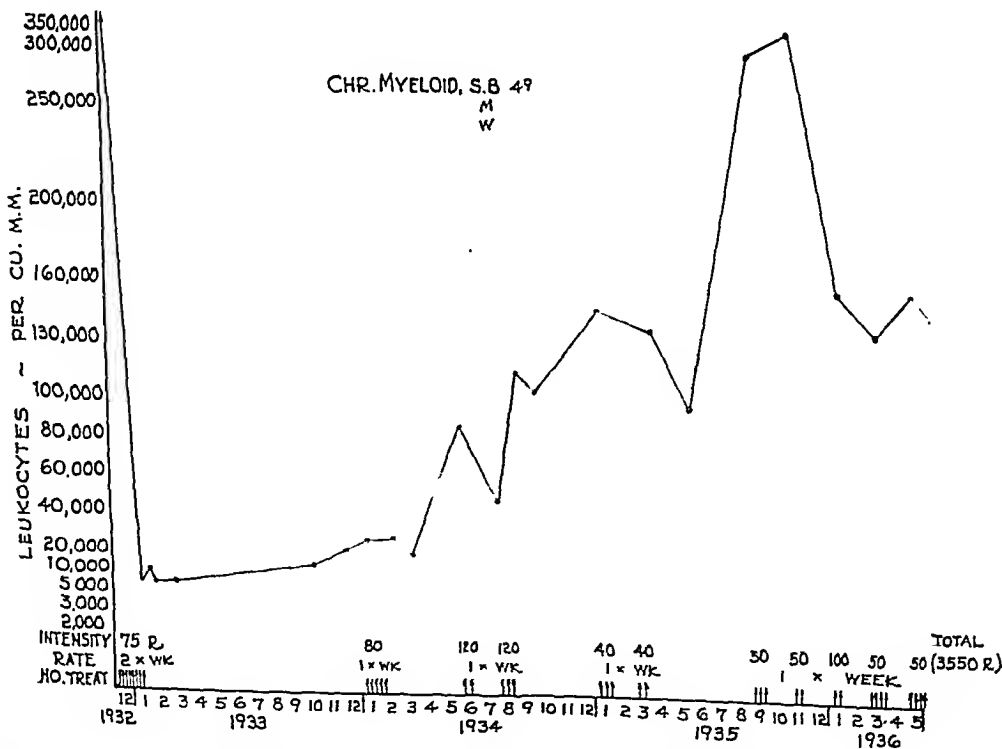


CHART XIV. Sensitivity to the effects of irradiation commonly diminishes. This is a variable factor, occurring from one to three years after institution of treatment.

but this was increased to 50 r in some cases. Localized treatment with small fields of 15 and 20 sq. cm. was generally employed and was found to be much more convenient, with results as gratifying as with irradiation to the entire body.

The variations of response to different technical factors, rate and intensity are so great that technical criteria must be determined and regulated for each patient.

In 3 cases of this series the leukocyte count dropped to 2,000, but rapid elevation occurred with relapses (Charts IV and XI). All 3 of these patients lived more than three years after these episodes. A leukopenia resulting from excessively large doses may be fatal.

The red blood cell counts varied widely in patients surviving several years or more. Fluctuations to levels as low as 2,000,000 were commonly observed. Regeneration may be expected with clinical improvement. A marked disproportion between the normal hemoglobin and red blood cell rate should be cause for alarm. This change was frequently seen in the terminal stages.

SUMMARY

Irradiation is a valuable palliative procedure. Improvement in health and strength, and very often restoration of an approximately normal efficiency, may be achieved in more than 50 per cent of patients suitable for treatment.

The life span is probably increased in a small percentage of cases, although estimations for statistical purposes may be misleading and should not be used as criteria of the value of irradiation.

The technical procedure should evolve from the smallest dose compatible with maintenance of a favorable clinical status rather than from reductions in the normal leukocyte level.*

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* For discussion see page 392.



HEMATOLOGICAL AND CLINICAL CHARACTERISTICS OF LEUKEMIA*

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THE leukopoietic system is made up of bone marrow, lymph glands, spleen, and reticuloendothelial cells in other organs. Here arise polymorphonuclear leukocytes, lymphocytes, and monocytes. Normally the formation of white cells is a very active but orderly process, so regulated that the total number per cubic millimeter of blood varies only within narrow limits.

Under abnormal conditions, as in many infections, the number of cells released from the bone marrow is greatly increased. This increase is manifested by an accumulation of cells at the site of infection as well as by a larger number in the circulation. However, as under normal conditions, there are no very immature leukocytes. Immature cells remain in the bone marrow or at the site of formation elsewhere. The normal span of life for a polymorphonuclear cell is three to four days and for a lymphocyte about twenty-four hours. Under normal conditions five to ten billion new polymorphonuclear leukocytes and an equal number of lymphocytes, as well as many monocytes, must be released from the leukopoietic system every twenty-four hours to compensate for those destroyed.

Leukemia is fundamentally a disturbance in leukocyte formation and thus concerns primarily the bone marrow, spleen, lymph glands, and reticuloendothelial cells. It is characterized by a disorderly multiplication of cells in the leukopoietic system. Usually there is an increased number of leukocytes in the blood stream. Immature cells are almost always present, even if there is no leukocytosis. The disease suggests a neoplastic process. The blood findings only reflect a loss of normal physiologic control and balance.

All leukocytes develop extravascularly from reticulum cells through a number of intermediate stages. The primitive blood cell derived from the reticulum cell is differentiated into myeloblast, lymphoblast, or monoblast. According to the polyphyletic viewpoint of white cell formation, the line of development is already determined when this differentiation has taken place, so that one blast cell cannot change into another. Thus, a myeloblast cannot become a lymphoblast or monoblast. It can give rise only to a neutrophilic, basophilic, or eosinophilic myelocyte, which in turn becomes a mature polymorphonuclear cell. Likewise a lymphoblast becomes only a lymphocyte, and a monoblast only a monocyte. Only mature cells are released into the circulation, although new leukocytes may be less mature than normal if there is an excessive need for new cells as in lobar pneumonia.

In leukemia the cells go through these same stages, but the formation of new cells is more rapid owing to some unknown stimulation or to the loss of influences which normally control growth of the leukocyte and its release into the circulation. In acute leukemia the cells are usually very immature. The marrow is hyperplastic and often filled with immature cells, while the leukocyte count in the circulating blood may be very low. This seems to be explained by the fact that immature cells reach the circulation with difficulty even in leukemia.

Immature cells are identified by certain histological characteristics. All blast cells are without granules in the cytoplasm, which is very basophilic and so appears a deep blue with Wright's stain. Myeloblasts,

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lymphoblasts, and monoblasts are difficult to differentiate but may differ slightly in size, in number of nucleoli, and in the staining reaction of the chromatin. Often the identification of blasts depends upon the "company they keep." If the blood film shows myeloblasts and other intermediate stages of polymorphonuclear cells, the chances are that any blasts present are myeloblasts.

The chromatin in the nucleus of an immature cell is a fine interlacing thread ("lace-net"), which stains much lighter than the chromatin in the normal mature nucleus. Nucleoli are usually present. As the cells mature, the chromatin changes into heavy basic-staining material. This is the principal change in the transition of a lymphoblast into a mature lymphocyte. As a myeloblast develops, granules, which are neutrophilic, eosinophilic, or basophilic, appear in the cytoplasm to form myelocytes. Later the nucleus becomes lobulated and filamented, the chromatin takes on mature staining reactions, and thus a mature polymorphonuclear neutrophilic, eosinophilic, or basophilic leukocyte develops. A monoblast develops azure granules in the cytoplasm and changes in the nucleus to become a monocyte.

A diagnosis of leukemia is made after a hematological and clinical study. Usually the blood examination shows a leukocytosis, although a leukopenia is common, especially in acute leukemia. In a recent detailed study of 250 cases of leukemia¹ the white cell count was found to be below 6,000 per cu. mm. in 27.6 per cent, from 6,000 to 10,000 in 6.8 per cent, and over 10,000 in only 65.6 per cent. Many ill patients never have a leukocyte count above 1,000. Usually the differential count reveals immature cells. In the myeloid leukemias these may be the intermediate stages and include myelocytes, promyelocytes, and metamyelocytes, as well as myeloblasts. Immature cells may be seen in different clinical conditions, but probably a blast is seen only in leukemia.

Often in leukemia too few white cells are

available for study to find many immature cells. Here concentrated preparations of leukocytes are of the greatest value. These are simply prepared by allowing the red cells to settle out by gravity for a short time, centrifuging quickly, and making films from the "buffy" coat, or layer of white cells on the surface of the red cells. In this way many white cells may be obtained for microscopic study, and blasts and immature cells are easily found. However, the cells in the circulating blood only reflect the activity of the tissues in which the leukocytes are formed. A biopsy of the bone marrow may be obtained by trephining the sternum or some other bone. In most cases, however, an entirely satisfactory specimen of the marrow may be secured by aspirating the sternal marrow with a large needle and making coverslip preparations from the aspirated material. When the diagnosis is difficult otherwise, leukemia may be disclosed by an examination of the marrow. In all doubtful cases a study of the bone marrow is mandatory.

Myeloid, lymphoid, and monocytic leukemia in which the predominant cell is of myeloid, lymphoid, or monocytic origin may occur in both acute and chronic forms. In 400 cases of leukemia seen during the past fourteen years in the hematology laboratory at the Cleveland Clinic the distribution has been as follows: (1) acute myeloid or myeloblastic, 16.5 per cent; (2) chronic myeloid, 24.7 per cent; (3) acute lymphoid or lymphoblastic, 15.3 per cent; (4) chronic lymphoid, 29.5 per cent, and (5) acute and chronic monocytic, 14 per cent. The disease is much more prevalent in men than in women. Sixty-one per cent of the 400 cases were men. Persons of every age are affected. In our series the ages varied from three and a half months to seventy-eight years.

Since lymphoid and reticuloendothelial cells are scattered throughout the body in many different tissues, the hyperplasia characteristic of leukemia affects almost all organs. Enlargement of the lymph glands, spleen, and liver is common. The

bone marrow is hyperplastic and accordingly is hypertrophied. The wide distribution of the disease is largely responsible for the widely varying clinical picture. Immature white cells may infiltrate any organ.

Toxemia is characteristic of leukemia, and certain symptoms are typical of toxemia. The more important are fever, loss of weight, sweating, anorexia, malaise, and joint symptoms. The exhaustion so common in all types of leukemia is due in part to toxemia and in part to anemia. In most cases the anemia seems to be due to overcrowding of the marrow spaces by leukopoietic overgrowth, thus preventing normal red cell formation. Toxemia by its depressing effect on the bone marrow, however, is often a factor in the anemia. Especially in acute cases the marrow may be even aplastic although immature, making the differentiation of primary aplastic anemia and leukemia most difficult. The aplasia can be explained only on the basis of the effect of toxemia on the bone marrow.

Anemia, hemorrhage, and infection are very common in leukemia. These result from the characteristic toxemia and infiltration of tissues.

Rarely does a patient have active leukemia without anemia. A hemoglobin as high as 80 per cent was found in only 24 of the 250 patients studied. Only 3 patients with acute leukemia had a normal hemoglobin. Most of the patients without anemia had chronic lymphoid leukemia. The anemia is due to a depression of bone marrow by the toxemia and an actual crowding out of red cells by the overgrowth of white cells in the marrow. The characteristic symptoms are weakness, dyspnea, and pallor.

The anemia may be of any type. Seldom, however, is a marked microcytic or hypochromic anemia encountered, unless blood loss has been severe. In many cases the anemia is definitely macrocytic, especially in the leukopenic patient, and pernicious anemia may be suspected. The macro-

cytosis of leukemia is not adequately explained. An increased size of red cells is looked upon as indicating a deficiency in supply or lack of use of the erythrocyte-maturing factor present in liver extract. In leukemia the supply of the specific maturing factor is evidently adequate, since the anemia is not influenced by giving more of the specific maturing principle. The disease probably interferes with utilization of the erythrocyte-maturing substance in the bone marrow. At times the anemia is hemolytic. The platelet count is very variable. This may be very high in chronic myeloid leukemia, but in acute leukemia the number of platelets is often so greatly reduced that thrombopenic bleeding occurs. The thrombopenia may be due to crowding out of the megalokaryocytes in the marrow or to depression of marrow function by toxemia.

Hemorrhage is a frequent symptom in leukemia. In about 10 per cent of the 250 patients abnormal bleeding was the most important symptom. The tendency to abnormal bleeding is due to platelet deficiency, to increased permeability of the vessels without thrombopenia, or to a combination of these two factors. Abnormal bleeding is commonly manifested as petechiae, especially in acute leukemia. Gross bleeding, such as in the brain or from the intestinal tract, is not uncommon. Cerebral hemorrhage is a frequent cause of death in chronic myeloid leukemia, in which the number of platelets is usually increased.

Infection occurs frequently in acute leukemia in which leukopenia is very common, and the number of mature polymorphonuclear cells in the blood and tissues is greatly reduced. When normal body tissues come in contact with bacteria, infection may result from a decrease in defense cells. The more common sites are gums, tonsils, and rectum. Both infection and toxemia are responsible for the fever, which is almost always present.

The clinical picture in all types of leukemia varies greatly owing to widespread involvement of almost all tissues of the body

and to the effects of toxemia. The acute leukemias run a rapid course. The white cells in the blood are very immature. Often most of the cells seen in a stained film are blasts. A detailed analysis has been made¹ of 50 patients in each of the types of leukemia, (1) acute lymphoid or lymphoblastic, (2) acute myeloid or myeloblastic, (3) chronic lymphoid, (4) chronic myeloid, and (5) monocytic.

Acute lymphoid leukemia occurs principally in children. Two-thirds of the patients in this group were under ten years of age. The disease is rare in older persons. I have been impressed with the frequency of skeletal pains in acute lymphoid leukemia. Several patients had a definite arthritis. One boy of seven had marked swelling of an ankle and intense pain in the legs. Involvement of most of the large joints confined him to bed for two months before admission. The arthritis was associated with fever and anemia. The outstanding clinical characteristics of the acute lymphoid group, however, are anemia and weakness and an abnormal tendency toward bleeding usually manifested by easy bruising. The spleen was enlarged in most of our cases. Often enlarged glands were complained of, but the enlargement was minimal. Perhaps this group conformed more closely to the textbook description than any of the other groups. When a child presents fever, anemia, easy bruising, and enlarged glands and spleen the diagnosis is usually acute lymphoid leukemia. Here again leukopenia is common, although very high counts are observed also. The anemia is usually severe. It is seldom macrocytic and often microcytic.

Acute myeloid or myeloblastic leukemia has much in common with the acute lymphoid type. The patients in this group were older, all decades from the first to the seventh being represented. Only 6 patients were under ten; the other cases were quite uniformly spread over the ten to seventy year interval. The presenting complaints were perhaps the most varied of all groups. Among these were "chills and fever," "big

spleen," "swelling of the face," "stomach trouble," "sore throat," "weakness," "pernicious anemia," "muscle and joint pains," "I can't eat," and "fever." Actual joint involvement is much less common than in the acute lymphoid type. The outstanding clinical features are anemia and fever. Abnormal bleeding may be prominent but is infrequent. Infection is not so common as it is in the monocytic group. Necrosis occurs but is uncommon. The leukocyte count is seldom high. Two-thirds of this group of 50 patients had a total leukocyte count under 10,000. In 3 cases no myeloblasts could be found in the blood, although the marrow showed the typical picture of acute myeloblastic leukemia. Less than half the patients had a palpable spleen. At times there was some general glandular enlargement.

In many instances *chronic lymphoid leukemia* is mild and runs a prolonged course, although here as always the disease ends fatally. It is a disease of older persons. I have never seen this type in a young person. Eighty-eight per cent of the patients in this group were over fifty years of age; only 3 were under forty-five. Often no blast cells were seen. Usually fragile cells or smudges were present and probably represented immaturity. Even in the mild chronic cases the bone marrow showed a high proportion of lymphoid cells. The total leukocyte count was usually high. Only 1 patient in this group had a count less than 10,000. Many patients had no anemia. This is the only type of leukemia which persists for any length of time without the development of anemia.

The clinical symptoms in chronic lymphoid leukemia also are often mild. Enlargement of glands and spleen may be the only abnormality complained of by the patient for a long time. Most patients who have had leukemia for any length of time belong in the chronic lymphoid group. This type not infrequently has been an incidental finding in the examination of patients for other conditions. Patients entering the Clinic for chronic cough, iritis, abdominal pain, rheumatism, pain in the

legs, headache, leukocytosis, bladder trouble, constipation, and "sick spells" have had chronic lymphoid leukemia. In most cases the outstanding clinical feature was enlarged glands or spleen. Weakness was relatively uncommon. Infection as a complication was seldom encountered.

Chronic myeloid leukemia is characterized principally by weakness. This is partly due to anemia, which is almost always present, but the toxemia characteristic of the disease is also an important causal factor in the exhaustion. Many patients were concerned about an enlarged abdomen resulting from a marked splenomegaly. Fever is very common and was the presenting complaint in several instances. One patient was confined to a tuberculosis sanatorium for months because an acid-fast infection was suspected when the fever was really due to leukemia. The tendency to bleed is greater in the chronic myeloid than in the chronic lymphoid type, probably because of the more severe toxemia. Here the abnormal hemorrhage is not due to thrombopenia but to the toxemia effect of the disease on the endothelium of blood vessels. Usually the platelet count is high. Hemorrhage is not infrequently the cause of death. Infection is uncommon. In this group the patients' ages varied from two and a half to seventy-six years. Most patients were in the middle age group. In only 3 instances was the total leukocyte count less than 10,000. Usually the total count is high, and in over half the patients the count was above 100,000. Blasts were found in most cases.

The clinical picture of *monocytic leukemia* is more varied than that of any other group. Patients with monocytic leukemia complained most frequently of anemia or of weakness due to anemia. Anemia and weakness was the outstanding clinical feature in 19 of the 50 patients in this group. Fever alone or with anemia was also a prominent feature of the disease and was often associated with generalized body aching. Two other prominent symptoms were various types of infection and abnormal bleeding.

The infection most often involves the buccal tissues, so that the diagnosis can frequently be made from the condition of the gums and other tissues of the oral cavity alone. Hypertrophy of the gums is especially characteristic and may progress very rapidly, usually with necrosis. The necrosis may become chronic and persist for months. Other patients with equally typical monocytic leukemia, as far as the hematological diagnosis is concerned, may never have infection of any kind. Abnormal bleeding may be very severe and difficult to control. It is most likely to occur in patients with evident toxemia as manifested by fever and anemia and may progress rapidly. Bleeding here is usually the result of thrombopenia.

One patient was admitted recently to the dermatological service with multiple skin ulcerations previously diagnosed and treated as furunculosis. Leukemia was not suspected until the blood examination showed 20,000 leukocytes with many monocytes and monoblasts. Sternal puncture revealed a hyperplastic marrow with a great excess of monocytes. Severe anemia was present, and the patient had a persistent fever. Biopsy of a local lesion confirmed the diagnosis of monocytic leukemia. Another patient who had only a marked anemia during the course of his disease lived several years with multiple transfusions. There was no leukocytosis, although a high proportion of the cells were monocytes. The anemia was always macrocytic. Many other equally unusual clinical histories could be detailed.

The leukocyte count in monocytic leukemia is seldom high. Sixty per cent of the patients in this group never had a count above 10,000, and only 3 patients had a count above 100,000. The anemia was macrocytic in almost one-half the cases in which the volume index was measured. The youngest patient I have seen with leukemia was three and a half months old and had the monocytic type. One-half the patients in this group were over forty-five years of age. The spleen and glands were seldom enlarged. In some cases blasts were never seen.

SUMMARY

Leukemia is a disease of the leukopoietic system characterized by the loss of normal physiologic control of leukocyte formation.

Normally there is active orderly growth of white cells in the marrow, spleen, lymph glands and reticuloendothelial system. Only mature cells reach the blood stream.

In an acute need for defense against infection and toxemia the leukopoietic tissues can supply enormous numbers of mature cells. The hyperplasia, however, is still under normal physiologic control.

Normally five to ten billion polymorphonuclear cells and an equal number of lymphocytes are supplied daily. If needed, many times this number can be supplied.

In leukemia there is a disorderly overgrowth of leukopoietic tissues suggesting a neoplastic process. This is due either to some unknown stimulation or to a loss of normal physiologic control.

Leukemia is a generalized disease and may affect any part of the body. It is characterized primarily by toxemia and cellular infiltration of organs and other body tissues.

The bone marrow is always involved. It is usually hyperplastic but may be aplastic though immature.

The typical blood finding is leukocytosis with immature cells such as myeloblasts, myelocytes, lymphoblasts, monoblasts, and intermediate cells in the circulation.

Leukocytosis is, however, often absent, especially in the acute types. In the 400 patients the leukocyte count was below 10,000 in one-third of the patients. In 100 patients with acute lymphoid or acute myeloid leukemia the count was below 10,000 in over one-half the patients.

Anemia is almost always present, and thrombopenia is common.

The signs and symptoms of leukemia are principally the result of anemia, hemorrhage, and infection due to toxemia and cellular infiltration.

The greatest variety of clinical pictures is encountered, so that little is characteristic of a patient with leukemia.

Acute lymphoid leukemia is a disease of childhood. Anemia, bleeding, and arthritis are common symptoms.

Acute myeloid leukemia occurs in all ages and presents the greatest variety of symptoms and clinical findings.

Chronic lymphoid leukemia is often a very mild disease and runs a moderate though fatal course. Enlargement of glands and spleen is the outstanding feature.

Chronic myeloid leukemia is characterized by a marked toxemia causing almost constant fever and anemia.

Oral infections with hypertrophy of the gums are prominent symptoms in *monocytic leukemia*. The spleen is seldom palpable. The leukocyte count is usually not very high. The anemia is often macrocytic.

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DISCUSSION OF PAPERS BY DR. WIDMANN
AND DR. HADEN

DR. ROBERT S. STONE, San Francisco, Calif. It has been very interesting and instructive to listen to these papers on leukemia, since we radiologists must understand it both from the point of view of how to diagnose and treat it and from the point of view of its development in ourselves.

I was glad to hear Dr. Widmann bring out the fact that sometimes patients are overtreated and it would be better if we used smaller doses. I think that may be one thing that radiophosphorus will teach us, that it is possible to control some leukemias with smaller doses of radiation than are frequently used and that we should try to control them with the lowest possible dose.

An interesting point brought out by Dr. Haden is that one-third of the leukemic patients that he has treated did not have elevated white blood cell counts. We hear so frequently that the amount of radiation we give should be controlled by the white blood cell count. Dr. Widmann, I think, emphasized the point that we must regulate our treatment by the type of

symptom that the patient has rather than by the white blood cell count, and when you review charts such as he showed of the white blood cell count and the roentgen therapy, there may be no coördination between them at all because the treatments were given to control the symptoms and not to bring down a high white count.

I believe it is possible to cause leukemia by irradiation, and it therefore behooves us to watch more carefully the exposures that we are getting, that our technicians are getting and that industrial radiographers are getting if we wish to keep down the incidence of leukemia in those working with radiations.

DR. U. V. PORTMANN, Cleveland, Ohio. It is astonishing that many radiologists have forgotten the different types of normal blood cells, the forms present in the leukemias, and the anatomic location of the principal hemopoietic tissues. This is one reason why Dr. Haden was asked to review this whole subject for us in twenty minutes. He has done so admirably, and I am sure we have all profited.

Dr. Widmann, in a comprehensive manner, statistically reviewed his results in the treatment of leukemias and came to the conclusion that longevity is increased by roentgen therapy but pointed out also that longevity is not the only criterion for evaluating results. We often gain the impression clinically that many patients with leukemias given roentgen therapy live longer than they might if not treated. Also economic usefulness is undoubtedly prolonged and morale improved; therefore, we should not be discouraged about the results of roentgen therapy for these incurable diseases.

Dr. Widmann also pointed out that we should not attempt to establish routine methods of treatment but should consider patients individually. In my opinion this is most important. We should take into consideration the blood picture, the condition of the bone marrow, and the general condition of each patient as indicative of when and how much treatment should be given.

Some radiologists believe that irradiation is contraindicated when the white blood cell count is less than 40,000. We have not hesitated to treat patients with what is called a leukemia, depending more upon the types of abnormal cells found in the blood than upon the number. As Dr. Haden stated, we have treated many patients with white blood cell counts of less than 10,000.

Dr. Widmann and Dr. Stone gave timely warning that the dosage of roentgen radiation given at one time should be small.

DR. HENRY J. ULLMANN, Santa Barbara, Calif. There are one or two points in Dr. Widmann's paper that I wish to discuss, and with which I heartily agree. One is the question of producing irradiation sickness referred to every once in awhile in articles on leukemia. I, personally, cannot see the slightest excuse for making any patient with leukemia sick with the roentgen ray. If one does so, too much has been given.

A point that I have never heard spoken of is what I call "coasting." My method is similar to Dr. Widmann's: that is, small doses repeated as indicated by the blood count, and, if I am treating every day with, let us say, 50 r (and when I use the term r it means total skin dose, or r on the skin), a count is made each day before the treatment is given. This is important, because after a patient's blood count begins to fall, it may continue to coast downward, in some instances for several days, and if one is treating a patient with only a 10,000 to 12,000 white blood cell count, one must watch for that "coasting."

I am tremendously interested in the total polymorphonuclear count in these patients, for I treat a leukemic with very minute doses, even as low as 25 r, measured on the skin, when the count is as low as 6,000, if the total polymorphonuclear count is very low or absent, which means the immediate danger of a terminal infection. Conversely, I might not treat a patient who felt perfectly well with a count of 25,000 if there were plenty of polymorphonuclears.

At the meeting of the American Medical Association in 1940 Dr. Forkner spoke of a thrombocytopenia being produced by roentgen irradiation. I have never heard of it. I would consider such a result the sequence of gross overdosage or recklessness. The platelets usually rise as the red blood cell count rises.

DR. W. EDWARD CHAMBERLAIN, Philadelphia. I just want to ask Dr. Haden to comment upon the difficulties that we have been having in differentiating between acute lymphocytic leukemia and acute leukemia of the myelogenous group. The hematologists seem to have a great deal of difficulty in this regard and we have sort of had the feeling that perhaps all

the acute leukemias would have to be grouped together with a big question mark as to how many of them are of the lymphocytic group and how many of them are of the myeloid group.

DR. ERICH M. UHLMANN, Chicago. It seems that we are all agreed that in dealing with leukemia the patients and the disease have to be treated and not the white blood cell count or any other symptom. On the other hand, laboratory tests may be of importance in timing the treatments better than it would otherwise be possible. In the past five years we have utilized the determination of the basal metabolism rate for such purposes. It is not a new discovery but it has been known for over forty years that the basal metabolism may be elevated in leukemic patients. In our material this is true in over 60 per cent of all patients treated for lymphatic or myelogenous leukemia. If the basal metabolic rate is elevated, its repeated determinations may be used as an excellent index to begin and terminate treatments. I will give you an illustration.

In 1939 a patient previously treated for lymphatic leukemia presented himself for follow-up examination. He was at that time in excellent health, had a white count of 14,000 cells, a normal differential count, no lymphadenopathy, and no other clinical signs of leukemia. A routine determination of his basal metabolism, however, revealed a rate of 69 per cent. Since the patient felt perfectly well, the possibility of an error was considered, and the test was repeated one week later. The second determination showed 71 per cent, and the patient was kept under close observation. Check-ups on the basal metabolic rate at weekly intervals showed no change, but four weeks after the first test, generalized lymphadenopathy developed, the patient grew continuously weaker, and within two more weeks the white blood cell count rose to 160,000. Following roentgen therapy instituted at that time, the basal metabolic rate dropped within three weeks to 16 per cent, the white blood cell count decreased to 120,000, but the lymphadenopathy showed little change. Roentgen therapy was then discontinued in order to observe the course of the disease. Within one month, the white blood cell count dropped to 18,000 and all clinical symptoms disappeared.

We have observed similar occurrences in about 20 patients since that time, a number of

whom were reported before the Radiological Society of North America two years ago. These patients have been followed now over a five year period and of the reported group, none have died during this time. This may, of course, be only a coincidence but it might also be attributed to the fact that these patients were treated with extremely small amounts of radiation which were sufficient to control the disease and not too high to render the patients resistant to repeated roentgen treatment.

DR. CHARLES L. MARTIN, Dallas, Texas. Will Dr. Haden be good enough to discuss the condition known as agnogenic myeloid hyperplasia? I have never made this diagnosis, but several authors have stated that it can be confused with leukemia, and that the use of roentgen therapy may be disastrous.

DR. HADEN (closing). There are two or three things to be emphasized again. One is that leukemia is not a disease of the circulating blood; it is a disease of the leukopoietic system. This is the reason I object very much to gauging treatment entirely on blood studies because you need all the information possible concerning the entire leukopoietic system.

Take for instance the cases of Dr. Portmann. A leukopenic leukemia with a marked hyperplasia of the marrow should be treated as vigorously as if the person has a count of a million white cells. What you are treating is the hyperplasia in the marrow, not the cells that have actually got into the blood stream.

One important point has not been mentioned—about the time to start treatment. I am an internist and not a radiologist, but I think it is a great mistake to treat patients with leukemia by irradiation too early. Many patients can be carried on easily for quite a long time before irradiation is begun.

It makes no difference how high a person's white blood cell count is. The treatment is *not* curative. You are trying to make the patient have a feeling of well being.

So much in leukemia depends upon the toxemia, of which anemia is probably the best index. A progressive anemia is always an indication for more aggressive treatment. Many hematologists would much rather know what the hemoglobin content is rather than the white blood cell count in treating leukemia.

Determination of the basal metabolic rate has

not helped us much in managing leukemia. A leukemia may be very active without a high metabolic rate.

Dr. Chamberlain has asked how to differentiate acute lymphocytic leukemia and acute leukemia of the myelogenous group. That is a very embarrassing question for a hematologist, but in most cases if one sees the patient from both the blood and clinical standpoint (and it has been my good fortune to see them in both the laboratory and in the clinic), one can usually be fairly sure whether the disease is lymphoid or myeloid in origin. The general pattern of the cells present helps greatly. An immature cell is a lymphoblast, a myeloblast, or a monoblast. What kind of company does that cell keep? One can usually tell by the bone marrow findings and other cells present the origin of

the immature cell better than by the characteristics of the individual cell.

Dr. Martin asked about agnogenic myeloid hyperplasia. After all, the marrow is a very hyperactive part of the body. Think of the billions of white blood cells that are formed every day, the great speed with which they are circulating and being destroyed! Agnogenic myeloid hyperplasia is a terminal state in which the normal physiologic control is lost and abnormal cells get into the circulation. This is not leukemia, and there is no reason whatsoever to treat such cases as leukemia.

I wish very much that the word "aleukemia" were dropped entirely from the terminology of hematology. Cases so designated are really examples of leukopenic leukemia. Why call them aleukemia?



A ROENTGEN STUDY OF CHRONIC PULMONARY COCCIDIOIDOMYCOSIS

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ALTHOUGH coccidioidomycosis in its malignant disseminated form was recognized as a clinical entity as early as 1892 by Wernicke and Posadas of Argentina, it is only in the past decade that the far more common benign or "primary" form of disease has been recognized. For many years it had been known that the incidence of erythema nodosum was much higher in the San Joaquin Valley of California than in other parts of the country. When associated with an influenza-like respiratory infection the disease was variously referred to as San Joaquin Valley fever, valley fever, desert fever, or desert rheumatism. All patients were thought to recover. In 1935 Gifford¹² and Dickson⁸ were able to demonstrate that *Coccidioides immitis* was the causative organism in this disease. Dickson thereupon suggested that the name "coccidioidomycosis" be employed for both forms of the disease, classifying as primary, the acute initial infection, and progressive or secondary, the classical coccidioidal granuloma.

Up to 1936 the total number of cases of coccidioidomycosis reported in California was only 450 of whom 224 had died. Yet Dickson found by sending a questionnaire to 75 physicians practicing in the San Joaquin Valley that a total of 354 patients with valley fever associated with erythema nodosum had been seen in the previous eighteen months (January, 1936–May, 1937). All but one of these patients had recovered spontaneously. In a similar period (December, 1937–May, 1939) Dr. Charles E. Smith of Stanford, investigating the disease in Kern and Tulare counties, saw 432 cases of acute coccidioidomycosis with erythema nodosum or erythema multiforme. The illness in every case was associated with either a positive sputum

culture or a positive coccidioidin skin test. Gifford and her associates found by testing 2,718 school children in Kern County that 55 per cent gave positive coccidioidin skin tests. The percentage rose from 17 per cent for those of less than one year residence in the county to 77 per cent for those having lived in the county ten years or more. In one group of 143 positive reactors only 4 gave a history of erythema nodosum; in another group, only one of 76 positive reactors had had erythema nodosum. Smith calculated on this basis that the 432 cases with erythema nodosum that he had seen must have represented some 8,000–10,000 infections. Thus, a high incidence of coccidioidal infection of the population, particularly of the subclinical type, was demonstrated in this endemic area.

With the advent of war and establishment of Army Air Fields throughout the endemic Southwest, the military implications of coccidioidomycosis were quickly appreciated, and a control program was set up under the Army Air Forces Western Flying Training Command. It was decided to skin test all new personnel arriving at Army Air Fields under this command. Negative reactors were retested six months later. Chest roentgenograms on positive reactors were carefully rechecked for any evidence of the disease. In addition, a syllabus on coccidioidomycosis was prepared and distributed in 1942 to all Army Air Fields in the Western Flying Training Command. All Medical Corps officers of these Fields were alerted to recognize the disease. As a result, several hundred clinical cases were discovered, as well as several thousand subclinical cases having a positive coccidioidin skin test. All clinical cases were hospitalized until evidences of activity had disappeared. All were checked periodically by roentgenograms. In most cases, the

acute febrile illness was self limited and of short duration, but a small percentage of infections persisted for many weeks or months, and a few terminated fatally. Patients whose infections were unusually prolonged or severe were generally transferred to the Santa Ana Army Air Base Regional Hospital for further observation and care. This group forms the basis of the present study.

ETIOLOGY AND EPIDEMIOLOGY

The causative organism was at first thought to be a protozoan. Rixford and Gilchrist, in reporting the first 2 California cases in 1896, so described it. In 1900, however, Ophuls and Moffitt were able to demonstrate its fungus nature. The name, *Coccidioides immitis*, suggested in 1896 by Dr. Charles Wardell Stiles then of the Bureau of Animal Industry, was retained nevertheless.

In its parasitic stage, as seen in tissue sections, the organism is a spherule 5 to 80 or more microns in diameter with a thick double contoured refractile capsule. It enlarges as it matures, and its granular protoplasm breaks up into a large number of endospores which are released when the spherule bursts. The released endospores then enlarge independently to form mature spherules, thus repeating the cycle.

The vegetative phase appears as a cottony white fungus which grows with great freedom on many media. It reproduces by budding and fragmentation of the mycelia. Although it is readily cultured in the laboratory, little is known of its occurrence in nature. It is generally assumed that the fungus grows in the soil or on vegetation during the rainy season and that during the dry season the chlamydospores break from the fungus and are scattered with the wind. This theory is in accord with the known seasonal incidence of the disease which is lowest during the rainy months of December to May and highest during the dry months of August to October. Those whose work brings them in close contact with the soil are most apt

to become infected, such as farmers, fruit and cotton pickers, linemen, well diggers, and others. Davis, Smith and Smith⁶ reported a group of seven Stanford students who developed the disease after digging out a rattlesnake in the Panoche Valley. *Coccidioides* was recovered from the soil of the rattlesnake nest. Emmons¹⁰ suggests that small rodents such as pocket mice and kangaroo rats may be an important natural



FIG. 1. Acute pneumonic type of coccidioidomycosis, lower right lung; complete resolution within three weeks. Symptoms: malaise, mild substernal pain, cough. Temperature 99-100° F., six days. Leukocyte count 8,700, with neutrophils 78 per cent, eosinophils 2 per cent. Sedimentation rate 50. Coccidioidin test positive.

reservoir for the disease. In a high percentage of these animals coccidioidal organisms could be isolated from the characteristic nodular lung foci.

All observers are agreed that direct person to person transmission of the disease does not occur. The disease is acquired almost solely by inhalation of air contaminated by chlamydospores. Rarely, direct infection through abrasions of the skin have been reported, but no case of infection via the gastrointestinal tract has been recorded.

The disease is endemic throughout much of the arid Southwest including the great central valley of California (the San Joaquin) especially south of Fresno, the

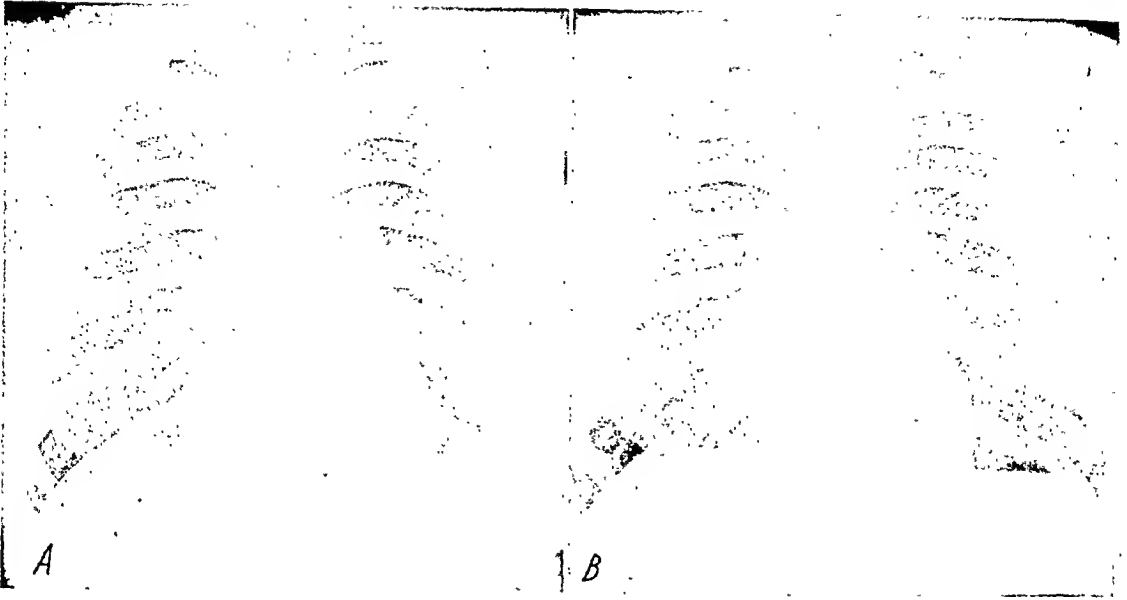


FIG. 2. *A*, coccidioidal pneumonitis, left base. Symptoms: fever, backache, substernal and lower left chest pain, five days, asymptomatic thereafter. Coccidioidin test positive. Complement fixation test positive 1:2. *B*, nodular coccidioidal focus with small central cavity, left base, at site of pneumonitis shown in *A*, twelve days later. Patient asymptomatic. Lesion unchanged over a three and one-fourth month period of observation.

whole of Arizona but especially the regions about Phoenix and Tucson, Southwest Nevada, and parts of New Mexico and Western Texas. Sporadic cases have been reported from the Midwest, Idaho, Utah, the Chaco region of Argentina, Bolivia, Paraguay, Brazil, Northern Mexico, Hawaii and Italy.

ACUTE PRIMARY COCCIDIOIDOMYCOSIS

After a period of ten to fourteen days following inhalation of air contaminated with coccidioidal spores, the patient may, or may not, have clinical symptoms. Most residents of endemic areas never develop symptoms of any kind, the only evidence of the disease being a positive coccidioidin skin test. Others develop an acute febrile illness often misdiagnosed as a severe "cold" or "flu" or "pneumonia." The patient complains of backache, headache or general aching, of marked weakness, loss of appetite and various indefinite gastrointestinal disturbances. Cough begins early and is usually of a dry irritating type, but small amounts of sputum may be raised. A most striking feature, and especially signifi-

cant in differentiating the disease from the more common respiratory infections, is the occurrence of chest pain in a very high percentage of individuals (87 per cent of one series of 30 acute cases). This varies from a dull constricting substernal type to a very sharp knife-like pain which may suggest coronary occlusion or even fractured ribs. Tenderness to pressure is often encountered over the painful area. The temperature is of a spiking type with afternoon rise, usually to 100° to 102° F. The white count is elevated in most cases averaging 10,000 to 12,000 (6,000-16,000), the neutrophil percentage is mildly increased and eosinophilia of 3 to 15 per cent may be present. Usually after three to ten days the temperature falls to normal, and the patient feels well except for weakness and perhaps residual chest pain. Then, one to two weeks later, painful nodules may develop on the shins and elsewhere characteristic of erythema nodosum. In other cases, macular, papular or vesicular lesions of erythema multiforme may appear. Acute arthritis and conjunctivitis are often associated with these allergic skin manifesta-

tions. The skin lesions are said to occur in 2 to 5 per cent of all cases,²⁰ but the incidence is evidently much higher in clinically diagnosed cases (19 per cent of 85 cases reported by Goldstein and MacDonald¹³; 17 per cent of our series). Following the acute illness the patient frequently feels weak and easily fatigued for many weeks or months thereafter.

A roentgenogram of the chest taken at the time of hospital admission will show characteristic roentgen findings in at least 4 out of 5 patients. Infiltrations vary in extent from the slightest fuzzy thickening of hilar shadows to extensive consolidations occupying one-third to one-half a lung field. These infiltrations are mostly unilateral, homogeneous, usually hilar or basal in location and show little tendency to lobar distribution. They vary in density from the lightest veil-like haze to consolidations approaching but rarely equaling that of lobar pneumonia. The appearance resembles that of the primary atypical pneumonias, being more uniform, less patchy, more circumscribed than the usual bacterial bronchopneumonias. The hilar type infiltration resolves most rapidly, usu-

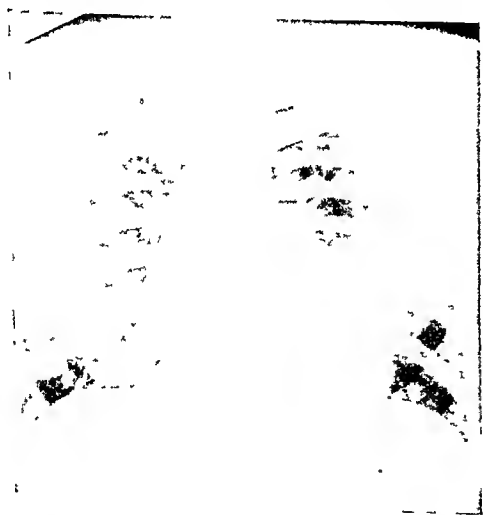


FIG. 3. Nodular coccidioidal focus, left mid-lung, unchanged over eight month period of observation. Sputum originally positive for *Coccidioides immitis*. Coccidioidin test positive. Patient asymptomatic except for occasional sharp left chest pains; leads active, normal life.

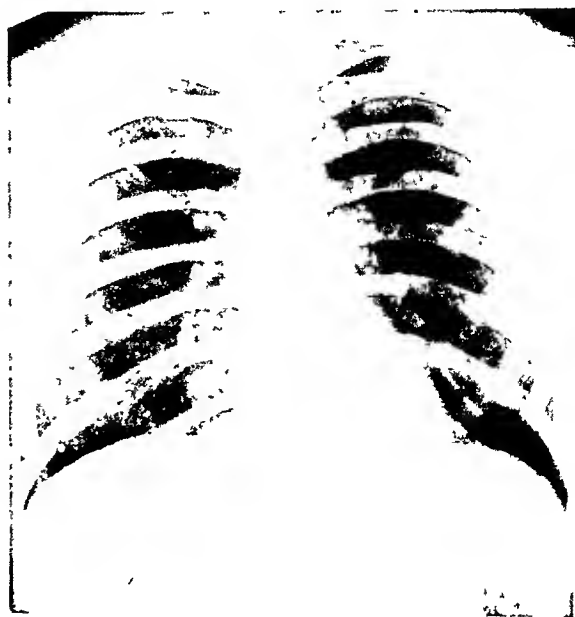


FIG. 4. Nodular coccidioidal focus, right apex, unchanged over nine and one-half month period of observations. Discovered on routine roentgenogram. Coccidioidin test positive. Occasional chest pain, slight cough.

ally within one to two weeks. The very soft parenchymal infiltrations also resolve rapidly and completely, usually by the second to fourth week, while the denser consolidations generally clear more slowly and give rise to a majority of the persistent infections. Mediastinal or hilar adenopathy occasionally accompanies the more severe of these acute primary infections, but when it does occur, it is usually transitory and mild in degree. Pleural effusion is encountered in approximately one-fifth of all acute primary cases but ordinarily is so small in amount as to scarcely fill the costophrenic angle; it resolves rapidly and completely.

DIAGNOSIS

The diagnosis of coccidioidomycosis depends on (1) a positive coccidioidin skin test plus a diagnostically characteristic roentgenogram and a compatible clinical history, (2) positive serologic tests, or (3) recovery of the fungus from the sputum (or, in disseminated cases, from accessible nodes or abscesses). Kessel¹⁵ and others have shown that the coccidioidin test has a

high degree of specificity and parallels in many respects the tuberculin test in its mode of action. A positive reaction indicates that the patient has had at one time a coccidioidal infection, and does not necessarily imply that a present illness is due to this infection. On the other hand, a negative test excludes the disease in all but terminal cases.

Serologic tests have proved a very valuable aid, both from the standpoint of diagnosis and prognosis. Precipitin and complement fixing antibodies appear in the blood early in the course of the disease. Usually in the early stages precipitins are present in higher dilution but rapidly disappear. The complement fixation titer falls off more gradually. With resolution or focalization of lung infections, complement fixation disappears or is present in low dilution; with dissemination, the titer remains at a constantly high level or increases to the "danger" range of 1:64 to 1:128 or more.

Recovery of the fungus from the sputum is a difficult and tedious process, and in

acute primary cases the sputum is often so scanty as to make this procedure impractical. Examination of sputum under a coverslip in the fresh state is very unsatisfactory, since fat droplets and other artefacts may readily simulate the organism. Culture on Sabouraud's medium followed by guinea pig or mouse inoculation is the only reliable method of recovering and identifying the organism.

PERSISTENT COCCIDIOIDAL INFECTIONS

In cases with persistent coccidioidal infections the clinical picture parallels quite closely the findings shown by roentgenogram. Persistent infections may thus conveniently be classified and discussed according to predominant roentgen manifestations, as follows:

1. Nodular parenchymal foci.
2. Cyst-like cavities.
3. Persistent pneumonitis.
4. Mediastinal and hilar adenopathy.
5. Pleural effusion.
6. Miliary lung involvement, metastatic.

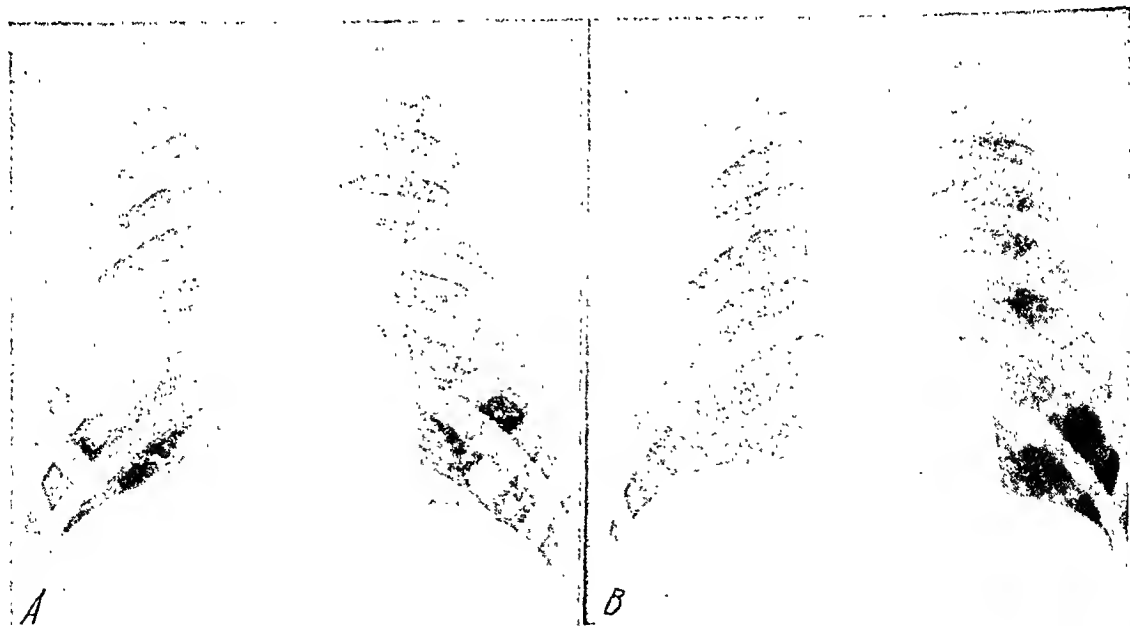


FIG. 5. *A*, coccidioidal pneumonitis, right mid-lung. Infiltration had largely but not completely cleared on roentgenograms taken two weeks later. No further roentgenograms were taken until ten months later. *B*, coccidioidal cavity, right mid-lung, at site of pneumonitis shown in *A*, twelve and one-half months later. *Coccidioides immitis* recovered from the sputum. Coccidioidin test positive.



FIG. 6. *A*, coccidioidal cavity, right subapex, discovered on routine roentgen examination. Patient asymptomatic. Coccidioidin test positive. *B*, coccidioidal cavity shown in *A* beginning to disappear eight months later.

bone foci and other evidences of dissemination.

Of 96 cases of persistent infection followed at the Santa Ana Army Air Base Regional Hospital for periods of from two to twenty-one months, 23 cases were of the nodular type, 35 were cyst-like cavities, 21 were persistent pneumonites, mediastinal adenopathy was predominant in 2 cases, pleural effusion was outstanding in 3, and the remaining 12 cases were disseminated. Only those patients whose roentgenograms showed evidence of infection beyond a two month period, constituting some 10 to 15 per cent of clinical cases, are included in this group of persistent infections.

NODULAR PARENCHYMAL FOCI

The nodular parenchymal foci were discovered, in a majority of cases, on routine roentgenograms. Fifteen of the 23 cases of this type were so discovered. Of the 15 cases, 3 were found on questioning to have had occasional chest pains, 4 had felt weak and easily fatigued, and the others had been symptom free. Eight gave a history of an acute febrile illness two to ten months

previously. Three additional cases were discovered by chest roentgenograms taken because of patient's complaint of chest pain in 2 instances and abnormal fatigability in the other. The coccidioidin skin test was positive in all these cases, the temperature was normal in all, and sedimentation rate was mildly elevated in only 3 cases. Complement fixing antibodies were present in low dilution in 2 of 6 cases in which it was tested for.

Only 4 patients were followed directly through from a preliminary stage of pneumonitis to nodule formation. In all 4 cases the initial acute illness was of relatively short duration and comparatively mild symptomatically. Temperatures varied from 99° to 101° F. and lasted three to seven days. Infiltrations, which at first were more or less diffuse, tended to round out with decrease in size leaving solitary well circumscribed nodules at the sites of the previous zones of pneumonitis. The elapsed time from the initial pneumonitis to nodule formation varied from ten days to three months, averaging five to six weeks.

The nodules in all but one instance were

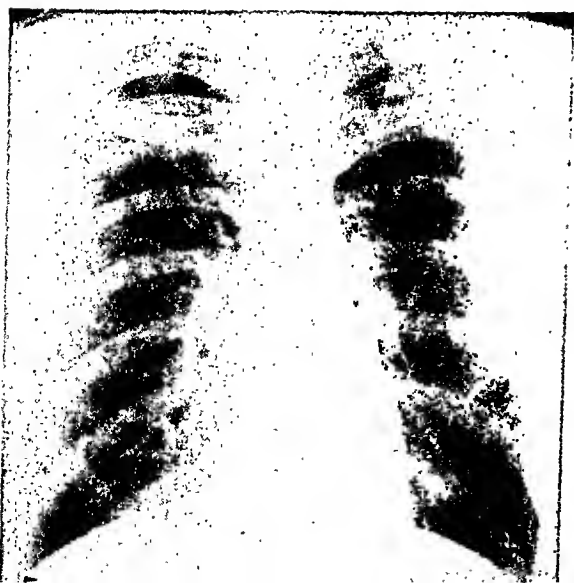
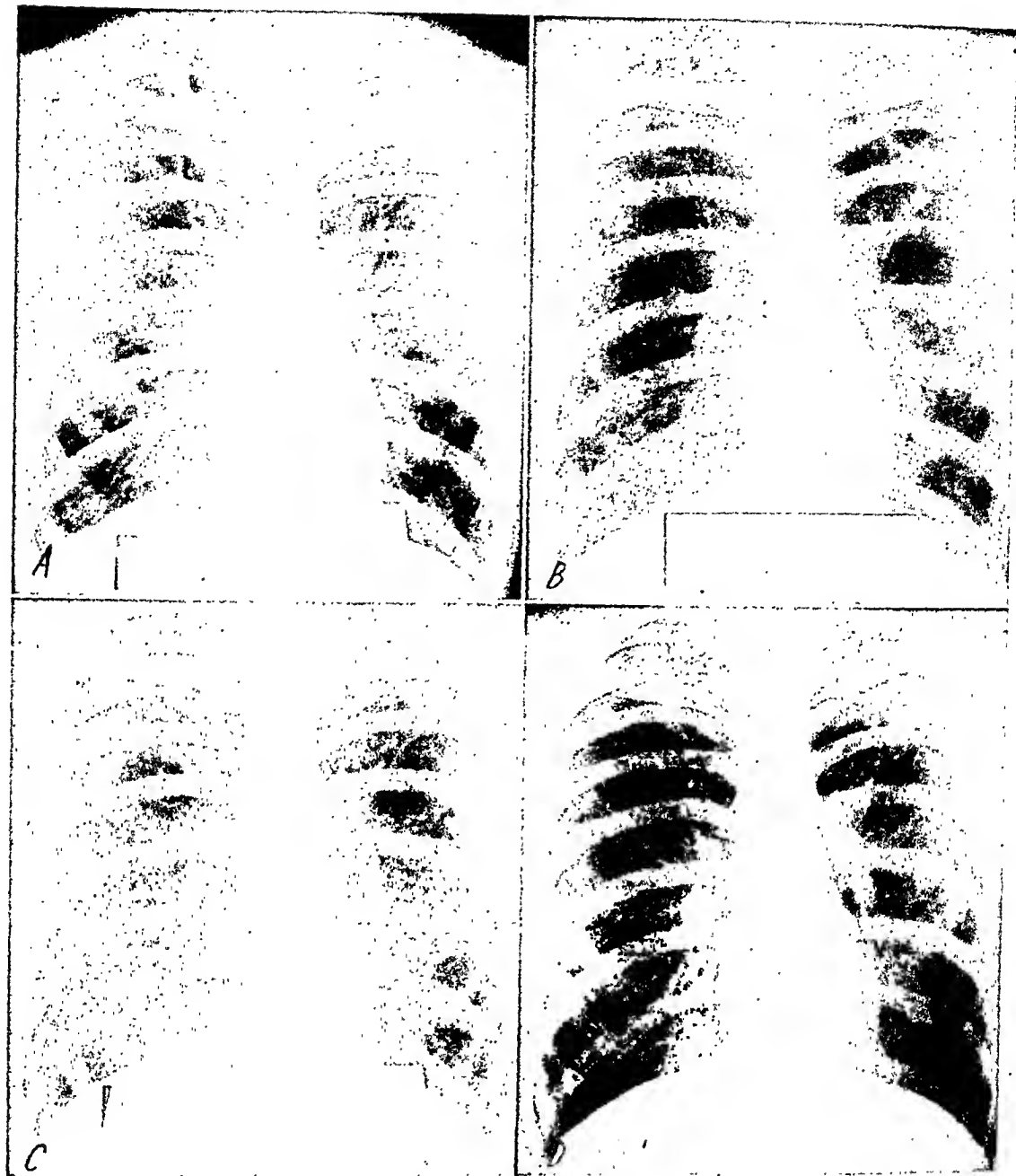


FIG. 7. *A*, small coccidioidal focus, left apex, discovered on routine roentgenogram. Patient practically asymptomatic, slight cough. Normal temperature. Coccidioidin test positive. Complement fixation test positive 1:4. Sedimentation rate elevated five months, normal thereafter. *B*, coccidioidal cavity, left apex, four and three-fourths months after *A*. *Coccidioides immitis* recovered from sputum. Patient remained essentially symptom free, raised small amounts of purulent sputum. Temperature normal. Leukocyte count 5,000 to 11,700, eosinophils 11 to 14 per cent. *C*, coccidioidal cavity shown in *B* much smaller three months later. *D*, re-enlargement of coccidioidal cavity two months after *C*. *E*, coccidioidal cavity shown in *D* had disappeared after three weeks.

single. They were located in the apical or subapical regions in 2, the mid-lung in 12, the lower lung in 7, and were multiple and generalized in one. They averaged 2.0 cm. in diameter, varying from 0.8 to 4.2 cm. They were strikingly similar in appearance to solitary neoplastic metastases, or uncalcified primary tuberculous foci. In the 1 case in which multiple nodular foci were present the resemblance to extensive metastatic malignancy was pronounced. In this instance, however, each of the nodular lesions was preceded by a zone of pneumonitis, and some of the nodules later developed central cavitation.

The period of time that the nodules were under observation was insufficient to give a clue as to their ultimate fate. Over an average observation period of six and one-half months (one to nineteen months) only a single one of these foci had disappeared, four had decreased an average of 3 mm. in diameter and the remaining seventeen had changed not at all. From other studies, however, it is evident that some, at least, go on to eventual calcification. *Coccidioides immitis* has been recovered from calcified pulmonary nodules at autopsy (Cox and Smith⁴). Aronson and his coworkers¹ found a high incidence of calcified nodules in Indian children living near Phoenix, Arizona, who failed to react to tuberculin but did react to coccidioidin. Failure to react to tuberculin in those showing calcified nodules could not be attributed to anergy since in 56 of 62 such persons the tuberculin test became positive one year after the intracutaneous injection of B.C.G. vaccine. The inference was strong that these calcified nodules were coccidioidal in origin.

COCCIDIOIDAL CAVITIES

Coccidioidal cavities, like the nodular foci described, are frequently discovered on routine chest roentgenograms without prior clinical evidence of disease. Thirteen of 35 cases were so discovered. Five of the 13 were found on questioning to have had occasional chest pains or had felt weak and under par. Six additional patients were

discovered to have cavities by roentgenograms taken because of symptoms of chest pain in 3, hemoptysis in 2, and weakness and fatigability in one. In 11 cases, cavity formation was seen to follow directly on a preceding stage of pneumonitis. In 5 additional cases, cavities were observed to develop by central excavation of pre-existing nodular foci.

The acute illness preceding cavity formation was generally more prolonged and



FIG. 8. Persistent coccidioidal pneumonitis, left apex. Lesion discovered on routine roentgenogram. Patient asymptomatic. Temperature normal. Acute febrile illness with erythema nodosum, four months previously. Coccidioidin test strongly positive. Tuberculin test negative. Sedimentation rate 10-20. Lesion unchanged over eight and one-half months of observation.

severe than in cases later developing nodules. Temperatures varied from 100° to 103° F. and averaged nine days in duration. The acute symptoms of severe malaise, cough, chest pain, general aching, and so forth, were generally present over a two to four week period, subsiding thereafter, usually coincident with the appearance of cavities as shown by the roentgenogram. That such cavities then represent latent focalized infections is shown by the fact that, in the great majority of cases, temperature, white blood cell count and sedimentation rate fall to normal limits, and antibodies disappear from the blood or remain in low dilution soon after the cavity

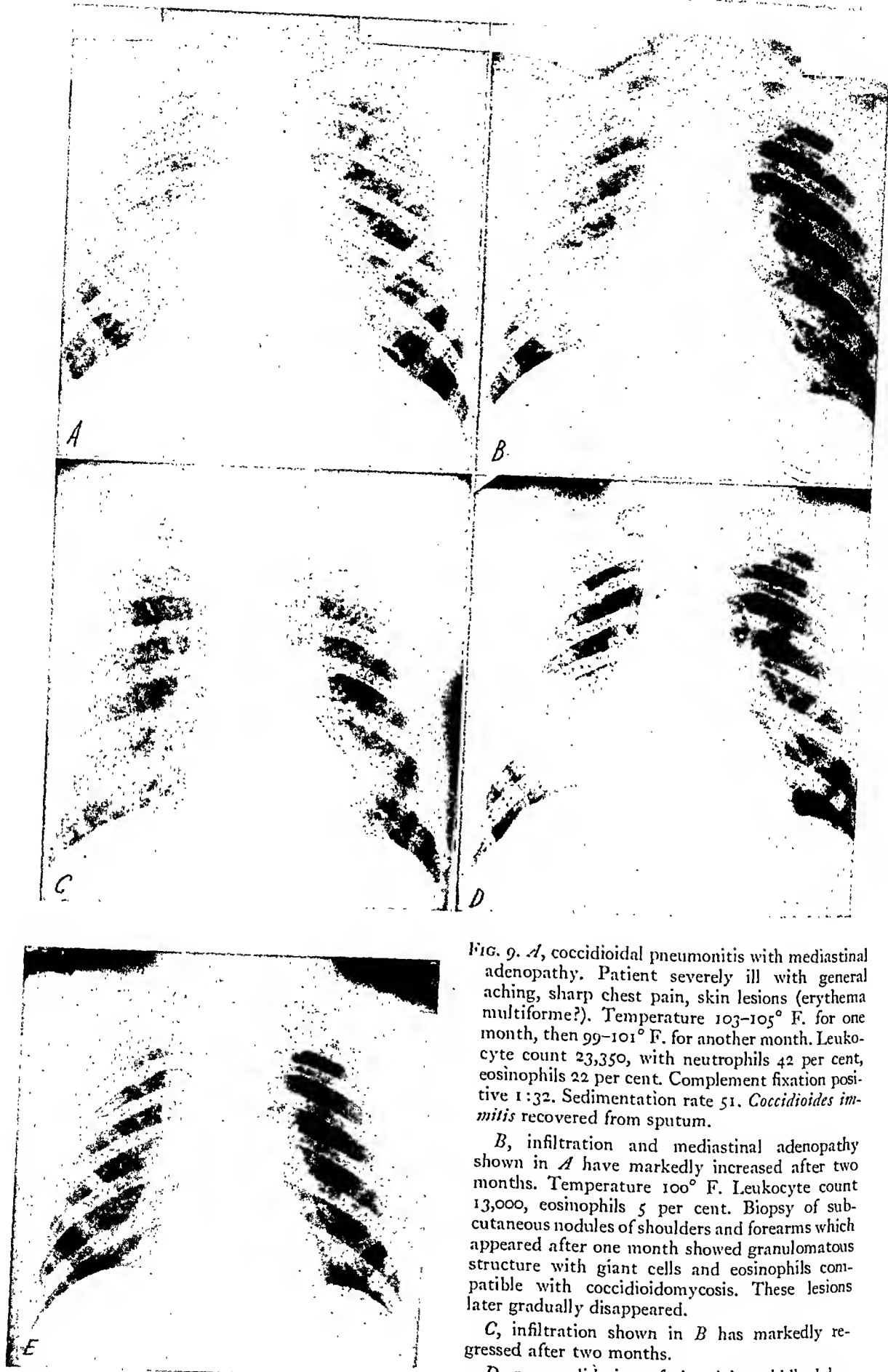


FIG. 9. *A*, coccidioidal pneumonitis with mediastinal adenopathy. Patient severely ill with general aching, sharp chest pain, skin lesions (erythema multiforme?). Temperature $103-105^{\circ}$ F. for one month, then $99-101^{\circ}$ F. for another month. Leukocyte count 23,350, with neutrophils 42 per cent, eosinophils 22 per cent. Complement fixation positive 1:32. Sedimentation rate 51. *Coccidioides immitis* recovered from sputum.

B, infiltration and mediastinal adenopathy shown in *A* have markedly increased after two months. Temperature 100° F. Leukocyte count 13,000, eosinophils 5 per cent. Biopsy of subcutaneous nodules of shoulders and forearms which appeared after one month showed granulomatous structure with giant cells and eosinophils compatible with coccidioidomycosis. These lesions later gradually disappeared.

C, infiltration shown in *B* has markedly regressed after two months.

D, re-consolidation of the right middle lobe, four months after *C*, nine months from onset of

coccidioidomycosis. Patient returned from leave with headache, chest pain, cough, temperature $100-103^{\circ}$ F.

E, infiltration shown in *D* has cleared after one and one half months. Adenopathy has largely disappeared. Complete recovery.

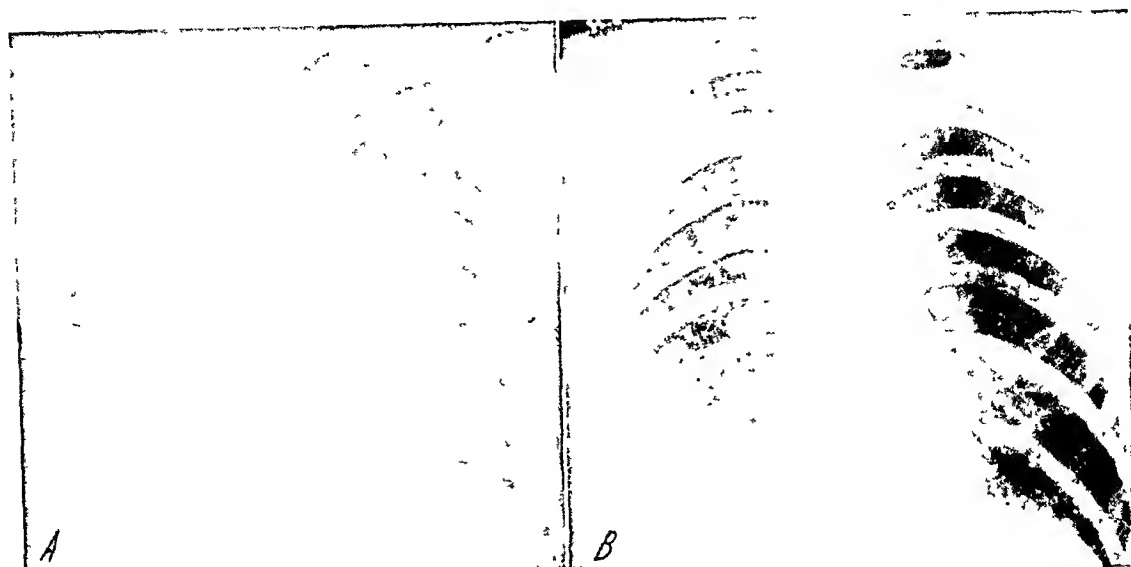


FIG. 10. *A*, massive coccidioidal pleural effusion. Coccidioidin and complement fixation tests positive. Right chest pain. *B*, effusion shown in *A* has decreased after four months. No parenchymal infiltration demonstrated at any time.

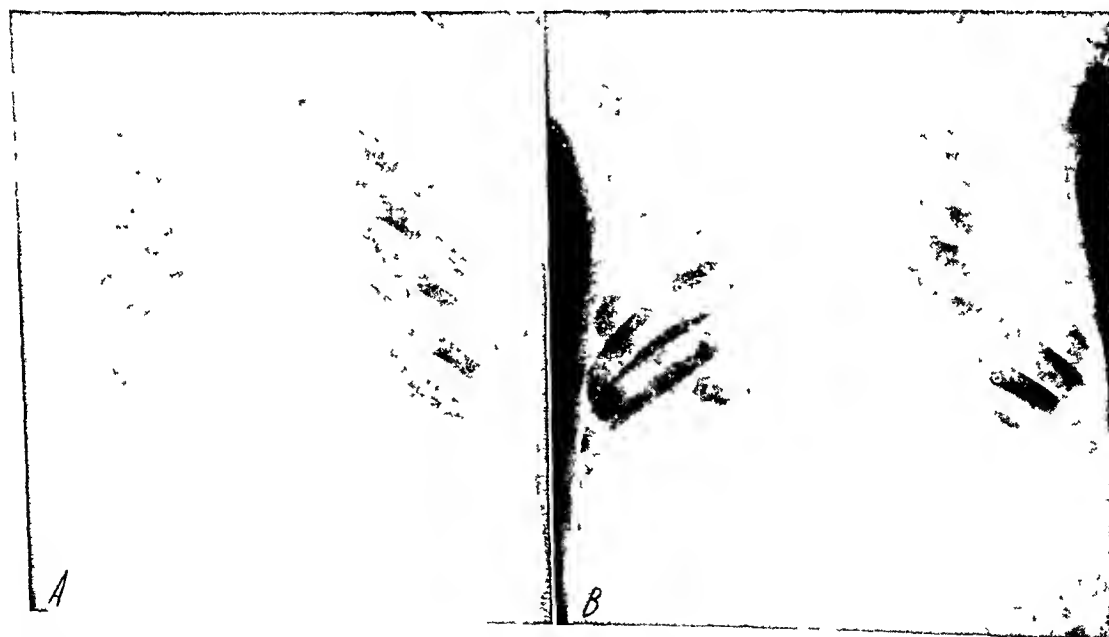


FIG. 11. *A*, small amount of coccidioidal pneumonitis at left costophrenic angle and right mediobasal region with mediastinal adenopathy. Negro admitted with complaints of feverishness, fatigue, malaise, tender "lumps" 3-5 cm. in diameter on lower chest, sternum, abdomen and extremities. Temperature 102-103° F. Complement fixation titer as high as 1:128; sedimentation rate as high as 98. *Coccidioides immitis* recovered from subcutaneous nodules by culture and guinea pig inoculation. *B*, extensive partly confluent miliary infiltrations with mediastinal adenopathy, two months after condition shown in *A*. Many punched out foci of bone destruction in ribs, scapula and humerus. Course steadily retrogressive with great weakness, severe weight loss, occasional headaches, and anorexia to time of death three months from onset.



FIG. 12. Massive mediastinal coccidioidal adenopathy. Negro admitted with fever, headache, general malaise, anorexia, followed by persistent cough, marked weakness and wasting, dull pain in mid-chest, and cervical adenopathy. *Coccidioides* recovered from cervical nodes. Died in coma seven months from onset. Temperature 101-103° F., leukocyte count 13,000-17,000 with neutrophils 68 per cent; erythrocyte count 3.6 million, hemoglobin 83 per cent. At autopsy necrotic mediastinal nodes found to have eroded into esophagus. Also involvement of meninges, kidneys and heart.

appears. Moreover, clinical signs of activity are usually absent even in presence of considerable fluctuations in cavity size and wall thickness. About half the patients, however, complain of persistent weakness or intermittent chest pain so long as a cavity is present. Four of our patients developed hemoptysis with their cavities, and the fungus was recovered from the sputum in 6 of 11 cases in which this procedure was attempted.

Infiltrations preceding cavitation were homogeneous zones of consolidation 2 to 10 cm. in diameter which tended to round out with decrease in size prior to excavation. The average elapsed time from the appearance of infiltration to development of cavity was three and one-half weeks (ten days to eight weeks). Mediastinal adenop-

athy accompanied 4 of the 11 precavity infiltrations but, in each case, disappeared as the cavities developed.

Cavities were single in every case, located in the upper lung field in 11, the mid-lung in 15, and the lower lung field in 9 cases. Most cavities were of a very thin-walled type without surrounding infiltration, presenting a characteristic ring-like or cystic appearance. Cavities which developed through central excavation of nodular foci were usually smaller in size and thicker walled having a doughnut-like appearance. These cavities required an average of three months to develop (one to six months).

All cavities were remarkably indolent, slow in evolution, and benign in character. But minor fluctuations in size and wall thickness were recorded in practically all cases. In 8, the fluctuations were of such degree and occurred so rapidly as to strongly suggest ballooning due to air trapping. The cavities were followed roentgenographically for periods of from one to eighteen months, averaging seven and one-half months for the group. During this time only 10 cavities had disappeared, 6 had ended as small nodules and the remaining 19 were essentially unchanged.

The manner in which cavities disappeared was of some interest. Often one side of the wall would appear to melt away leaving a crescentic residuum which then gradually resolved. Some of the larger thinner walled cavities appeared to collapse rapidly over a period of several days either to reappear just as suddenly or to disappear permanently. Less commonly, the cavity gradually diminished in size ending as a small nodule. The 19 cavities still present after an average follow-up period of seven and one-half months were actually slightly greater in average diameter (though thinner walled) than at the time of initial examination. They varied in size from 1 to 8 cm. in diameter, and averaged 2.2 cm. at the onset, while at the time of final observation, the average diameter was 2.6 cm.

Most coccidioidal cavities are so charac-

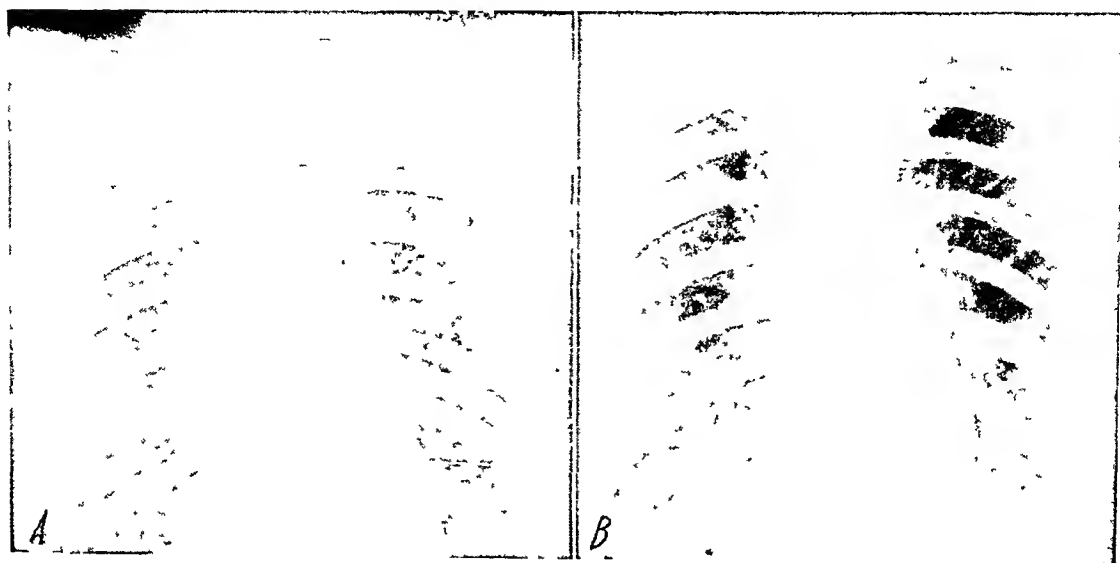


FIG. 13. *A*, mediastinal adenopathy with slight hilar infiltration. White patient admitted with malaise, headache and vomiting. Temperature 100° F. Leukocyte count 9,850, with neutrophils 65 per cent, eosinophils 10 per cent. Sedimentation rate 18-57. Coccidioidin test positive. Increasing headache followed by disorientation and mental confusion. *B*, mediastinal adenopathy and hilar infiltration shown in *A* have disappeared after two and three-fourths months. Patient died of meningitis one week later, three months from date of admission. Mediastinal nodes completely caseous but only slightly enlarged.

teristic in roentgen appearance that they are seldom confused with other conditions when occurring in endemic areas. They have been misdiagnosed as congenital cysts, and in 1 case a lobectomy was performed under this impression. Sante and Hufford¹⁹ have recently described annular lung shadows appearing in pyogenic blood infections which appear remarkably like those of coccidioidomycosis. Three of our 35 coccidioidal cavities contained fluid at intervals, and when fluid containing, were surrounded by infiltration. The appearance at these times resembled that of lung abscesses. Five other cavities which did not contain fluid but were surrounded by infiltration at various times could readily have been mistaken for ulcerative tuberculosis, especially when occurring in the upper lung fields.

PERSISTENT COCCIDIOIDAL PNEUMONITIS

A number of acute primary infiltrations failed either to resolve completely or to focalize as nodular or cystic lesions during the two to six week period usually re-

quired for resolution or stabilization. These patients, as a group, were clinically severely ill with marked prostration, malaise, general aching, usually sharp chest pain, and occasionally blood streaked sputum. Temperatures frequently reached levels of 103° to 104° F. during the first several days and persisted thereafter at lower levels for weeks or months (six days to three months: average twenty-nine days). Sedimentation rates were elevated to levels of fifteen to fifty for one to eight months (four and one-half month average). Complement fixing antibodies were present in dilutions of 1:4 to 1:32 initially, falling off after two to six months, and disappearing in all but the most severe infections after six months.

The initial infiltration was often extensive. In 7 of 21 cases consolidations occupied one-third to one-half the lung field, half were moderate in extent (4 to 8 cm. in diameter), while in 5 of the group, infiltrations were small in amount and limited to the hilar regions.

As might be expected, the more extensive, denser infiltrations were slowest to resolve, requiring six to twenty-one months

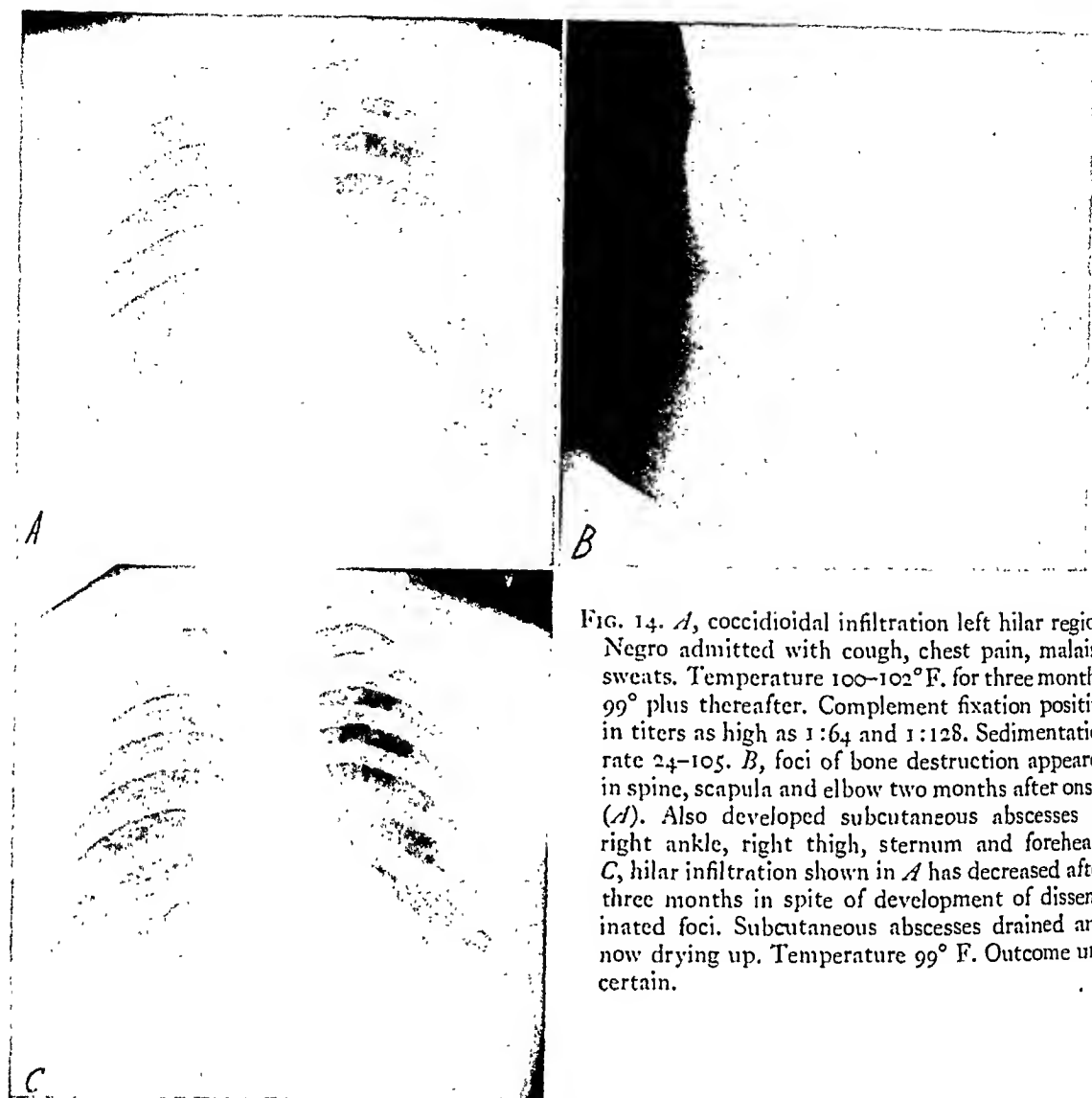


FIG. 14. *A*, coccidioidal infiltration left hilar region. Negro admitted with cough, chest pain, malaise, sweats. Temperature 100-102° F. for three months, 99° plus thereafter. Complement fixation positive in titers as high as 1:64 and 1:128. Sedimentation rate 24-105. *B*, foci of bone destruction appeared in spine, scapula and elbow two months after onset (*A*). Also developed subcutaneous abscesses at right ankle, right thigh, sternum and forehead. *C*, hilar infiltration shown in *A* has decreased after three months in spite of development of disseminated foci. Subcutaneous abscesses drained and now drying up. Temperature 99° F. Outcome uncertain.

to clear, while the smaller hilar infiltrations disappeared after an average interval of three and one-half months. In most cases, resolution was a very gradual but continuous process. Four of the group, however, showed exacerbations and remissions over periods of from four to ten months. In spite of the slow resolution, only 1 of the entire group of 21 showed evidence of fibrosis; the other infiltrations preserved to the very end a soft homogeneous or patchy appearance. Mediastinal and hilar adenopathy accompanied 6 of the 21 persistent infections of this group. In these cases it was of pronounced degree and exceedingly persistent (two to twenty-one

months; average eight months), often outlasting the parenchymal infiltration.

MEDIASTINAL ADENOPATHY

In 2 cases, marked mediastinal adenopathy, was the only roentgen evidence of disease. Both might readily have been misdiagnosed as Hodgkin's disease from the roentgenograms alone. The clinical illness was moderately severe. Complement fixation was present in titer of 1:16 to 1:32, and the sedimentation rates were at levels of thirty to fifty-four so long as adenopathy persisted, which was two and one-half months in 1 case and three months in the other.

PLEURAL EFFUSION

Pleural effusion was the outstanding characteristic of 3 cases. One of these patients, although developing fluid sufficient to produce complete opacity of one side of the thorax, never at any time showed evidence of parenchymal infiltration. A second developed moderate fluid after an initial transitory basal infiltration. Fluid persisted with fluctuations over a fourteen month period, during which time the temperature was elevated to 99° to 100° F. about one-third of the time and the titer of complement fixation rose as high as 1:128 in the range presenting danger of dissemination. The third patient developed slight pleural fluid in association with a coccidioid cavity. The cavity disappeared after four months, but fluid persisted and increased, lasting a total of thirteen months. The sedimentation rate was elevated the entire time and was as high as thirty-four after eleven months.

FATAL DISSEMINATED COCCIDIOIDOMYCOSIS

Cases destined to develop fatal dissemination cannot be distinguished at the onset from the usual acute pneumonic cases which subside in two or six weeks leaving no sequelae. Indications of impending dissemination are noted when the temperature fails to subside, the complement fixation titer, instead of decreasing rises to the dangerous heights of 1:64 to 1:128 and the sedimentation rate remains elevated at ranges of from fifty to one hundred. Usually within a few days or weeks of the onset of the acute illness, evidences of disseminated foci become manifest. Subcutaneous fluctuant areas 1 to 4 cm. in diameter may even be found at the time of initial hospital admission, and occasionally the presenting symptoms will be those of meningitis.

After the initial dissemination the course is usually that of progressive quiet cachexia to death some two to nine months later. The patient complains primarily of extreme weakness and fatigue and chest pain which is apt to be dull and central in type but may

be sharp and pleuritic. Cough is persistent and especially troublesome at night. Subcutaneous abscesses frequently break down discharging purulent exudate from which coccidioid organisms are easily recovered. Wasting is severe. The temperature remains elevated during the entire course of the disease, usually ranging from 101° to 103° F., but occasionally reaching levels of 104° to 105° F. White blood counts have varied from 7,500 to 27,200, averaging about 13,000, with neutrophils mildly increased and eosinophils ranging from 1 to 12 per cent. A secondary anemia of varying degree has been present in all cases averaging: hemoglobin 81 per cent, red blood cell count 3.8 million.

The roentgen picture in fatally disseminating coccidioidomycosis is dominated by mediastinal and hilar adenopathy. Parenchymal infiltrations, exclusive of the terminal miliary phase, were small in amount and limited to the hilar regions in 7 of our 9 fatal cases. In 4 of the 9, infiltration actually decreased during the later stages of the disease, and adenopathy decreased in 3 cases. Five of the group developed miliary seeding throughout the lungs during the final three to six weeks of their illness. This miliary infiltration developed, as a rule, much more rapidly, and less uniformly, than in tuberculosis and often became massively confluent. Individual miliary nodules tended to be less sharply circumscribed, more fuzzy in appearance than comparable foci of tuberculosis. Small punched out areas of bone destruction in the ribs, scapulae or clavicles could usually be found within a week or two of the appearance of the miliary lung involvement. The bone foci were similar in appearance to metastatic carcinoma.

The disease was found to be remarkably widespread at autopsy, involving practically every organ of the body. Tracheobronchial lymph nodes were invariably caseous and often showed liquefaction necrosis; mesenteric and cervical nodes were frequently caseous; the lungs were involved in all cases, 5 with miliary seeding,

but in 4 only small local foci could be found; foci of bone destruction were encountered in 7 of 9 patients. The incidence of involvement of other organs in the 9 fatal cases was as follows: spleen, 4; kidneys, 4; meninges, 4; liver, 3; heart, 3; adrenals, 1; pancreas, 1. The histopathologic appearance of individual miliary nodules was similar to that of pulmonary tuberculosis, being composed primarily of epithelioid and giant cells, but there were more polymorphonuclear and eosinophilic cells and more tendency to caseous necrosis than in tuberculosis, and many of the giant cells contained coccidioidal spherules.

DISSEMINATED NON-FATAL CASES

Three of our patients developed extrapulmonary dissemination which they were able to focalize successfully. Certain important differences were noted in these patients and those terminating fatally. In the first place, the clinical signs of activity, while often initially severe, soon diminished or even disappeared; temperature, sedimentation rate and complement fixation titer fell after a few days or weeks. Only 1 of the 3 had visible mediastinal or hilar adenopathy. Finally, the interval from original illness to first appearance of disseminated foci was considerably longer than in the fatal cases, averaging three months, whereas 7 of 9 fatal disseminated cases developed extrathoracic foci (subcutaneous abscesses, bone destruction, meningitis) within the first month of their illness, 4 within the first week.

FACTORS INFLUENCING DISSEMINATION

Individual and racial immunity are unquestionably the most important factors which determine whether or not a coccidioidal infection will disseminate. Smith²² states that the incidence of disseminated infection is four to seven times higher in males than in females. More important, the dark skinned races such as Negroes, Mexicans, and Filipinos show a much greater tendency to dissemination than do whites. On the basis of Army statistics, not yet

authorized for release, Colonel R. V. Lee¹⁶ has shown that fatally disseminating coccidioidomycosis is about one hundred times as likely to occur in a Negro as in a white person. Seven of our 9 fatal cases were in Negroes, only 2 in white persons. Thus the commonly accepted figure of 1 dissemination in 500 coccidioidal infections has no meaning unless related to specific racial groups. The incidence in dark skinned races is much higher.

Little is known as to the mechanism of immunity to coccidioidomycosis in humans. Emmons¹⁰ found a high incidence of circumscribed coccidioidal nodules in pocket mice and kangaroo rats but rarely endosporulating organisms. He demonstrated that suppression of maturation and endosporulation was due to host influence as shown by the fact that when strains of *Coccidioides immitis* from these animals were inoculated into more susceptible animals, endospores were invariably produced in the resulting lesions. Whether similar suppression of endosporulation occurs in resistant humans has not been demonstrated.

Smith²² has commented on the fact that dissemination, when it occurs in white persons, is more apt to be meningeal in type, whereas Negroes show a higher incidence of multiple subcutaneous abscesses. This observation is borne out in our group of fatal cases. Both deaths in white persons were due to meningitis, while subcutaneous abscesses were found in over half of the Negroes who died.

Roentgenographically, the one invariable finding in our disseminated cases of coccidioidomycosis was the presence of enlarged mediastinal nodes at least sometime during the course of the disease. At autopsy, the tracheobronchial lymph nodes were invariably caseous and often extensively necrotic and liquefied. Thus it would appear that the blood stream infection of disseminated coccidioidomycosis arises, at least in most cases, from caseous tracheobronchial nodes.

It would also seem that dissemination,

when it occurs early, as it does in most cases, is of more ominous significance than dissemination which occurs several weeks or months after the original acute infection. Carter² has commented on the relatively benign character of isolated foci which are started by minor injuries such as a bumped finger in apparently healthy individuals.

TREATMENT OF COCCIDIOIDOMYCOSIS

The treatment of coccidioidomycosis should correspond to the type and severity of infection. The acute benign form of the disease, constituting the great majority of cases, requires no other care than symptomatic treatment and bed rest until the lungs clear and sedimentation rate returns to normal. Patients with nodular foci should be allowed to carry on a normal active life. Patients with coccidioidal cavities require closer supervision and restriction of activities, but it is questionable whether prolonged hospitalization to time of cavity closure is necessary or advisable. Collapse therapy seems hardly justified in any of these cases with the exception of those patients with repeated and extensive hemoptysis. Patients who have persistent pneumonitis should be hospitalized until all clinical signs of activity (elevated temperature, sedimentation rate, complement fixation) have disappeared and mediastinal adenopathy, at least, has vanished completely. No form of treatment seems to materially affect the course of the disseminated cases. Bed rest, high vitamin and high caloric diet are certainly indicated, but all drugs so far employed have proved of no avail. Some claims have been made for vaccine therapy, but results have not been such as to inspire confidence to date.

SUMMARY

1. The history of coccidioidomycosis is briefly discussed, especially in regard to developments during the past decade. The epidemiology and pathogenesis of the disease are also briefly described.
2. The clinical features of the disease are discussed primarily from the stand-

point of differentiating and specific characteristics which distinguish the disease from other acute and chronic pulmonary infections. The coccidioidin skin test is shown to have a high degree of specificity and parallels the tuberculin test in its mode of action. Precipitin and complement fixation tests have proved valuable, not only from the standpoint of diagnosis but also as regards prognosis.

3. Ninety-six coccidioidal pulmonary infections which persisted for months or years following the acute initial phase of the disease are discussed according to predominant roentgen manifestation, as follows:

- (1) Nodular parenchymal foci.
- (2) Cyst-like cavities.
- (3) Persistent pneumonitis.
- (4) Mediastinal and hilar adenopathy.
- (5) Pleural effusion.
- (6) Miliary lung involvement, metastatic bone foci and other evidences of dissemination.

4. The roentgen findings are correlated with associated clinical history. Twenty-three nodular and thirty-five cystic foci were shown to be extremely indolent, benign in character and slow in evolution. Twenty-one patients with persistent pneumonitis required prolonged hospitalization over many months. Mediastinal adenopathy was the predominant roentgen characteristic of nine fatally disseminated cases until the terminal stage of miliary spread.

5. Factors which influence dissemination are discussed with emphasis on the racial factor. (Negroes are about one hundred times as likely to develop fatal disseminated coccidioidomycosis as white persons.) White persons are more apt to develop a meningeal type of coccidioidal dissemination, while Negroes show a higher incidence of subcutaneous abscesses. Dissemination, when it occurs late, appears to be of less ominous prognostic significance than when occurring within the first few days or weeks of the initial acute illness.

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THE MYELOGRAPHIC DIAGNOSIS OF EXTRA-MEDULLARY CERVICAL SPINAL CORD TUMORS*

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INTRODUCTION

THE usual roentgenologic approach to the diagnosis of tumors within the cervical spinal canal is a search for pressure effects on the vertebrae. The presence of an expanding lesion within the cervical spinal canal may be suggested by widening of the interpedicular spaces, destruction or rarefaction of the laminae and pedicles and changes in the interveterbral foramina, but these are usually late manifestations. Until quite recently myelography of the cervical spinal canal was considered a rather difficult, not to say hazardous procedure. The chief objections to the procedure were the possible entrance of lipiodol into the cranial cavity and the physical difficulties incident to roentgenoscopy and maintaining a patient in the inverted position. Pantopaque myelography³ makes it possible to explore further the cervical canal roentgenologically with an innocuous, slowly absorbable contrast medium, so that the diagnosis of intraspinal tumor masses in the cervical canal may be made before visible changes occur in the vertebrae. This communication reports the myelographic findings in 5 patients with extramedullary tumors of the cervical spinal cord or nerve roots in whom the direct roentgenograms were normal.

TECHNIQUE

Myelography of the cervical spine may be performed with a minimum of discomfort to the patient. A stock model motor-driven tilt table which may be tilted 10 degrees head downward and which is equipped for roentgenoscopy and spot film roentgenography is necessary. We believe it essential to obtain spot roentgenograms under roentgenoscopic control as quickly as

possible. The observer must always keep in mind the increased hazards to himself incident to prolonged roentgenoscopy and spot film roentgenography, and avail himself of all possible safeguards.

We have found 3 cubic centimeters of pantopaque injected into the lumbar subarachnoid space adequate. Others use 6 cc. and prefer to aspirate it after examination.⁵ The oil column must be maintained in as homogeneous a mass as possible. The patient, placed in the prone position with his face turned to one side, is first tilted so that the oil gathers in the lumbar sac. Then he is gradually inverted so that he is head downwards 10 degrees from the horizontal and the passage of pantopaque is watched roentgenoscopically. When this position is reached the oil column usually halts at the level of the first lumbar vertebra. The column may be advanced an additional 3 or 4 cm. by requesting the patient to strain.¹ When the pantopaque has reached the highest level it can with the patient still in this position, he is requested to assume gradually the knee-chest position, and the passage of the oil through the thoracic canal is watched. Streaking and globulation of the column can be kept to a minimum if the hips are gently elevated and the shoulders kept in contact with the table top so that the flow of oil through the thoracic canal is slow. Even though all precautions are observed it is not unusual for the column to break into large streaks and globules, and this should not be confused with organic disease. When the pantopaque reaches the upper thoracic region the patient is returned to the prone position and the table is tilted slightly caudad towards the horizontal. The oil is then permitted to collect

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in the lower cervical canal. As this region is entered the column first assumes a "U" configuration and then divides into two lateral ribbons of greater density between which the remainder of the oil collects. The "U" configuration is transitory and is not to be confused with intrinsic disease at the level of the sixth or seventh cervical vertebra.² If the axillary pouches are poorly outlined, they can be filled to better advantage by turning the patient's neck slightly into the oblique position. Occasionally the axillary sleeves fill poorly in normal spines, particularly when the flow of pantopaque through the cervical canal is rapid. Filling defects are considered of diagnostic importance only when confined to one region and when the other pouches are well visualized. The defect must be constant on successive studies.

The proper use of the 10 degree head downward position together with the knee-chest posture obviates the necessity of specially constructed tables or restraining devices or the aid of attendants for cervical myelography in patients who have no gross muscular disturbances. If the patient is cooperative it is possible for the roentgenoscopist to perform the examination without help and with very little discomfort to the patient. We have not achieved the same results with the knee-chest posture in the horizontal position, but others have reported better results.⁴ Patients with kyphosis or scoliosis of the thoracic spine cannot be examined in this way as a rule, but myelography may be readily accomplished if the patient is placed in a lateral position.

DIAGNOSIS

The diagnosis of cervical spinal canal tumors rests on the observation of the advancing head of the pantopaque column for filling defects. These may be transient, and may assume arcuate or curvilinear configurations. A definite lesion will produce the same deformity on successive examinations, and the observer must be sure that the spinal canal is adequately visualized on either side. Inasmuch as these filling de-

fects may occur as high cephalad as the foramen magnum, it is often impossible to prevent the passage of pantopaque into the basilar cisterns. As a rule, the oil can be returned promptly to the spinal canal by reversing the patient's position, and advantage may be taken of this procedure by observing the descent much the same as after a cisternal instillation.

REACTIONS

Thus far we have observed but two reactions which might be ascribed to the entrance of pantopaque into the basilar cisterns. The first occurred in a woman, aged forty-four, and started one week after cervical myelography, which was negative. She suddenly complained of intense vertigo which came on without warning and gradually diminished until it disappeared after four days. The second reaction occurred in a man, aged forty-six, who also had a negative cervical myelogram. He complained of intense headache which started five days after examination and gradually disappeared after two days. Lateral roentgenograms of the skulls of both patients showed droplets of pantopaque retained in the basilar cisterns.

REPORT OF CASES

CASE 1 (J. H. No. 231456). H. G., male, aged twenty-nine, complained of a sharp pain starting at the tip of the right shoulder and radiating down the flexor surface of the arm to the elbow. The pain, which started four months before admission, became gradually worse and was started or aggravated by exertion or strain. There was no weakness, paresthesias or loss of manual dexterity.

Physical examination revealed slight tenderness over the middle and lower cervical spine. Neurological examination was normal.

Cerebrospinal fluid examination revealed manometric indications of a partial block. The protein content was elevated to 107 mg. per 100 cc. The Wassermann reaction and colloidal gold curve were negative.

Anteroposterior, lateral, right and left oblique stereoroentgenograms of the cervical spine showed no bony change. The intervertebral spaces were normal. Pantopaque myelography

showed free passage of the oil to the level of the interspace between the fifth and sixth cervical vertebrae, where a transitory block occurred, after which the oil slowly trickled into the axillary pouches on either side. In the cephalad end of the oil column a small hemispherical defect convex caudad was noted overlying the spinous process of the fifth cervical vertebra.

A laminectomy uncovering the fourth, fifth and sixth cervical segments revealed a soft, gelatinous yellow-white tumor about 4 cm. long lying on the dorsal aspect of the cord attached to the posterior root of the right fifth nerve. The tumor entered but did not pass through the right intervertebral foramen. It was removed completely and the patient made an uneventful recovery.

Microscopic examination revealed a perineurial fibroblastoma.

CASE II (J. H. No. 277442). M. G., female, aged twenty-six, noted tingling in the second finger of her right hand, then intermittent aching pain in the right shoulder and drawing pains in the right arm for about two years before admission. After two months all the symptoms disappeared except for the tingling of the finger. A year later she noted paresthesias in her right arm, followed by twitching of both hands, numbness and increased sensitivity of both upper limbs. She began to limp on her right leg and had some difficulty in voiding for one month.

Physical examination revealed weakness of the right arm and leg, decreased tendon reflexes on the right side and diminished sensitivity to heat, cold and pin prick on the left side up to the level of the upper cervical segments.

Spinal fluid examination showed no manometric indications of block. The cerebrospinal fluid protein was elevated to 71 mg. per 100 cc. The Wassermann reaction and colloidal gold curve were negative.

Anteroposterior, lateral, right and left oblique stereoroentgenograms of the cervical spine showed no changes in the osseous or intervertebral structures. Myelography revealed a transitory, small hemispherical filling defect with the convexity directed caudad, in the advancing head of the oil column on the right side at the level of the interspace between the first and second cervical vertebrae. The pantopaque entered the basilar cisterns and emerged without delay when the patient was returned to the upright position.

Laminectomy exposing the first, second and third cervical segments revealed an encapsulated intradural extramedullary tumor about 2 cm. long and 1.5 cm. thick to the right and posterior to the spinal cord. About two-thirds of the tumor lay in the spinal canal and one-third extended into the foramen magnum. The tumor was removed and the patient made an uneventful recovery.

Microscopic examination revealed a psammomatous meningioma.



FIG. 1. Case II. Spot roentgenogram revealing a small hemispherical defect in the head of the pantopaque column at the level of the interspace between the first and second cervical vertebrae. Meningioma found at operation.

CASE III (J. H. No. 275513). R. N., female, aged fifty-five, first noted pain in the back of the neck about eighteen months before admission, followed by tingling in the fingers of both hands and progressive paralysis beginning in the right upper extremity, then the left upper limb followed by right lower and then left lower limb paralysis.

She had a complete tetraplegia when admitted, with her lower limbs held in a fixed flexed position. Physical examination revealed corresponding reflex changes, with complete loss of sensation to touch, pressure, pain, tem-



FIG. 2. Case III. Spot roentgenogram revealing an arcuate defect in the cephalad end of the oil column at the level of the interspace between the fifth and sixth cervical vertebrae. Meningioma found at operation.

perature, position and vibration over her entire body up to the level of the fourth cervical vertebra.

Cerebrospinal fluid manometric studies revealed a complete block. The total protein was increased to 490 mg. per 100 cc. The Wassermann reaction and colloidal gold curve were negative.

It was possible to obtain only an anteroposterior and lateral roentgenograms of her cervical spine, which were negative. Myelography, which was performed with the patient in the lateral position, revealed an almost complete block at the level of the sixth cervical vertebra, with a ribbon of oil trickling to the right of the spinal canal. At the cephalad end of the lateral ribbon overlying the right side of the interspace between the fourth and fifth cervical vertebrae there was a persistent arcuate defect concave caudad about 1 cm. wide.

Laminectomy uncovering the third to sixth cervical segments showed the spinal cord to be compressed to about one-sixth its usual size by a large intradural extramedullary tumor about 4 cm. long and 3 cm. wide. The tumor was solid,

pinkish in color, homogeneous and encapsulated, and attached to the dura at one point. It was enucleated and the patient was discharged markedly improved able to move all her limbs.

Microscopic examination revealed a psammomatous meningioma.

CASE IV (J. H. No. 273320). N. S., female, aged twenty-six, first noted pain in the base of her neck radiating down the right shoulder two years before admission. Numbness of the finger tips of both hands was noted one month ago, and the right arm became awkward and heavy in its movements. Transient twitchings of all four extremities was present, and she had difficulty in balancing herself on the right.

Examination showed moderate weakness of the right hand grip. Her gait was normal. The tendon reflexes were brisk, somewhat more marked on the right. The abdominal reflexes were absent, and the Hoffman and Babinski reflexes were pathologic bilaterally. There was marked stiffness of the neck, but no tenderness was elicited.

Cerebrospinal fluid examination showed normal manometric responses. The total protein was increased to 235 mg. per 100 cc. The Wassermann reaction and colloidal gold curve were normal.

Anteroposterior, lateral, right and left oblique stereoroentgenograms of the cervical spine showed no osseous or intervertebral changes. Pantopaque myelography revealed a partial block in the upper cervical spinal canal at the level of the first and second cervical vertebrae, where the head of the oil column swung from right to left and some of the oil entered the cisterna magna. A fluid level formed at the caudal end of the oil column when the patient was maintained in the inverted position. The left axillary pouch at the interspace between the second and third cervical vertebrae filled well, that on the right was not visualized.

Laminectomy of the second, third and fourth cervical vertebrae revealed a large subarachnoid extramedullary tumor extending from the top of the fourth cervical vertebra underneath the first cervical vertebra into the cranial cavity. The tumor was removed piecemeal. It was of mushroom shape, with the head extending into the cranial cavity and the stem extending alongside the spinal cord on the right occupying a lateral as well as an anteroposterior position down to the top of the fourth cervical vertebra.

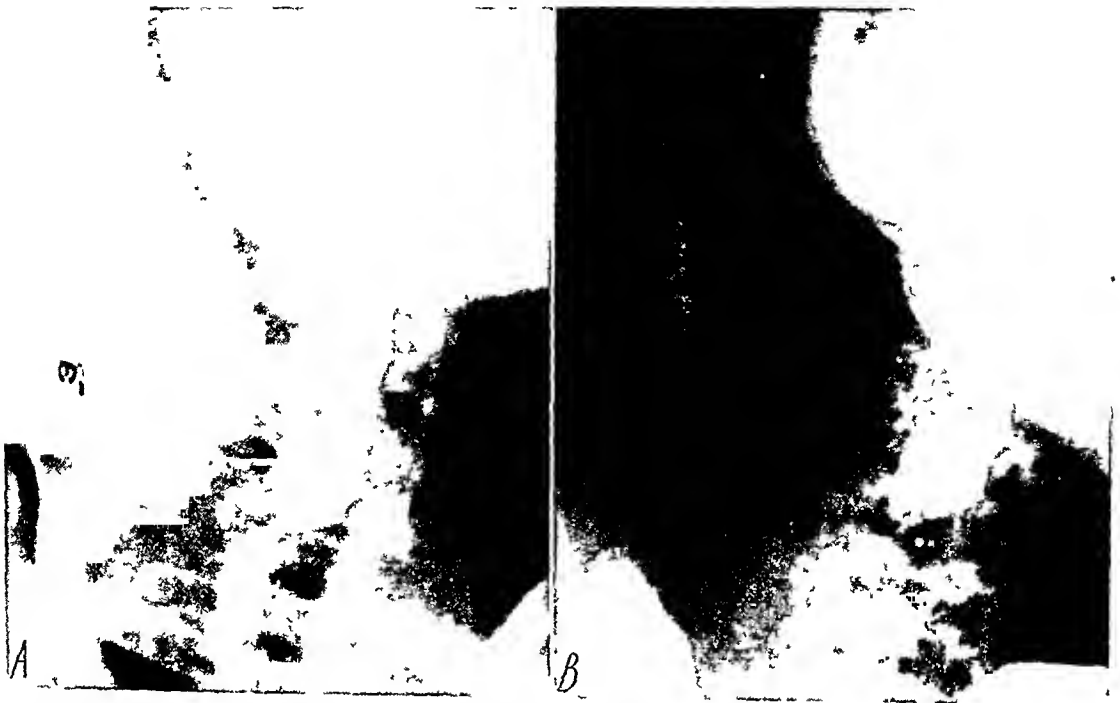


FIG. 3. Case iv. *A*, spot roentgenogram of lower cervical canal revealing normal configuration of the pan-topaque column. *B*, spot roentgenogram of oil column in upper cervical spinal canal revealing filling defect on the right at the level of the upper three cervical segments. Perineurial fibroblastoma found at operation.

The tumor was yellowish, glairy, soft and friable. The patient's recovery was uneventful and she was discharged relieved of symptoms.

Microscopic examination revealed a perineurial fibroblastoma.

CASE v (J. H. No. 271237). S. C., female, aged thirty-seven, first noted stiffness of her right leg about fifteen months before admission. Three months later weakness of her right hand appeared and progressed so that she was unable to hold anything. The condition improved somewhat after physiotherapy but soon recurred and was accompanied by weakness of the left hand and left leg for about three months.

Physical examination revealed active tendon reflexes bilaterally, with absent abdominal reflexes and a pathologic Babinski sign on the left side. A pathologic Hoffman sign was present bilaterally. The finer coordinated movements of the right hand were lost. There was past-pointing with both upper extremities. Impairment of temperature sensation was present in both lower limbs.

Anteroposterior, lateral, right and left oblique stereoroentgenograms of the cervical spine were normal. Myelography showed free



FIG. 4. Case v. Spot roentgenogram of upper cervical spinal canal revealing filling defect at level of upper two cervical vertebrae. Perineurial fibroblastoma found at operation.

passage of the oil through the lower cervical canal. The head of the oil column swerved sharply from left to right at the level of the first cervical vertebra, the caudal end forming a fluid level when the patient was kept in an inverted position.

Examination of the cerebrospinal fluid revealed manometric evidence of a complete block. The total protein was 52 mg. per 100 cc. The Wassermann reaction and colloidal gold curve were negative.

A laminectomy uncovering the upper three cervical vertebrae revealed an encapsulated extradural yellowish pink-gray tumor which was removed without difficulty. The patient made an uneventful recovery.

Microscopic examination revealed a perineurial fibroblastoma.

COMMENT

Four of the 5 patients were less than forty years old and one was fifty-five years old. The duration of symptoms was from fifteen months to two years in 4 patients, and four months in one. The onset of symptoms was insidious, and all noted pain in the back of the neck radiating to the shoulders. Four of the patients complained of pain in the right shoulder as an initial symptom, and it is conceivable that if the lesion were contralateral the pain may have simulated that encountered with coronary artery disease. Two patients had symptoms referable to the lower extremities, and 1 had a complete tetraplegia. The other 2 had no pain referable to the lower limbs.

There were 3 patients with tumors in the upper third of the cervical spinal cord, two of which extended into the cranial cavity, and two occurred in the lower third. The difference in the patterns of pain in the two groups was slight, and one could not definitely ascertain the level involved from the clinical picture alone. Thus, the first patient who had a perineurial fibroblastoma at the level of the fifth and sixth cervical vertebrae complained only of right shoulder pain with no other neurological signs, while the second patient who had a meningioma at the level of the first and second cervical vertebrae complained first of pain in the

right shoulder, then of changes in sensation of both arms and the right leg and diminished perception of pin-prick on the left side. The third patient, who had a complete tetraplegia had a lesion at the level of the sixth cervical vertebra. The fourth and fifth patients both had tumors at the first and second cervical vertebral level but presented dissimilar neurologic pictures. The fourth patient complained chiefly of neck pain radiating to the right shoulder, while the fifth complained first of pain in the right leg followed by weakness and pain first in the right hand and then the left hand and leg almost a year later. Essentially the pattern presented varied with the results of the pressure produced in each individual.

The most important cerebrospinal fluid finding was elevation of the protein content. Complete cerebrospinal fluid block occurred in 2 patients, 2 had a partial block and 1 had no demonstrable block. The presence of block appeared to be more dependent on the location of the tumor than on its size in the limits mentioned here.

Three of the tumors were perineurial fibroblastomas and two were meningiomas. They had in common the important fact that they were extramedullary and could be removed completely. All the patients recovered.

Complete direct roentgenographic examination was of no help. This is not always the case, perineurial fibroblastomas being frequently diagnosed because of widening of the affected intervertebral foramen and meningiomas often presenting the end-result of pressure on the laminae and pedicles of the adjacent vertebrae. Nevertheless, it is worth repeating that in this group of patients, who had tumors for as long as two years, no direct roentgenographic evidence of pressure effects on the vertebrae could be demonstrated on complete careful direct roentgenographic examination.

SUMMARY

Pantopaque myelography fills a gap in the diagnostic procedures available for the study of the cervical spinal canal. The ease

with which it may be performed and the richness of the information available make it a most important diagnostic method. It has already achieved widespread use in the identification of herniations of the nucleus pulposus of the lower cervical spine, and, as suggested by this report, may well be extended to the study of the upper cervical region.

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THE EHLERS-DANLOS SYNDROME*

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THE Ehlers-Danlos^{3,4} syndrome is an uncommon but well defined clinical entity consisting of (1) hyperelasticity and (2) fragility of the skin and blood vessels, (3) hypermobility of the joints, (4) pseudotumors over the bony prominences and (5) movable nodules beneath the skin. The disease is classified as a congenital dystrophic anomaly, but aside from the fact that it exhibits hereditary or familial tendencies,² little is known concerning its etiology. That the disease is probably a developmental error is supported by the frequent coexistence of additional anomalies. Synostosis of the proximal heads of the radii and ulnae,⁸ club feet,⁶ supernumerary teeth,⁵ congenital muscular atony¹² and delayed cranial ossification¹³ are some of the associated developmental faults which have been reported.

In describing the syndrome under the name *cutis hyperelastica*, Ormsby and Montgomery⁶ state that the soft velvety skin of these patients is loosely attached to the underlying tissues and, due to an actual increase in the amount of elastic tissue, the distensibility of the skin resembles that of animals. As a result, the skin may be grasped between the thumb and forefinger and extended in a rubber-like fashion as much as 3 or 4 inches, but in contradistinction to *cutis laxa*, it will resume its normal position when released. This startling hyperelasticity is generalized, but is most pronounced around joints. The hyperextensibility of the joints characteristic of this condition sometimes leads to spontaneous subluxations. It is actually possible for some of these patients to touch the dorsum of the hand with the finger tips of that same hand.

The hyperelasticity of the skin is associated with extreme fragility. Slight trauma produces large gaping wounds

which invariably leave rather characteristic linear or irregular papyraceous scars. Another unfortunate complication of relatively minimal injury is the formation of purplish, molluscoid pseudotumors over the various prominences of the body, particularly the elbows and knees. Skeer and Kaplan¹⁴ explain the development of these pseudotumors on the basis of extravasation of blood into the wounds produced by trivial injury. Eventually the traumatic hematomata undergo partial absorption, leaving masses of scar tissue which can be palpated through the skin. These masses are covered by semitranslucent membranes through which their coloring, resembling that of hemangiomas, can be seen.

Ronchese^{10,11} has emphasized that the four characteristic features of the symptom-complex under discussion may exist singly or in any combination, but as such cannot always be designated as the true Ehlers-Danlos syndrome. For example, many so-called "double jointed" persons have such a degree of hyperflexibility of their hands that they can subluxate interphalangeal articulations at will, although there is no associated abnormality of the skin. Hyperelasticity of the skin, either with or without excessive flexibility of joints, is an invariable finding in the "india rubber man" of side-show fame; increased skin fragility and its direct sequelae are notably lacking.

In 1934, Tobias¹⁵ submitted the first report of the Ehlers-Danlos syndrome in the United States, calling particular attention to an apparent associated abnormality identified by him as congenital lipomatosis. The alleged lipomata manifested themselves as relatively small, firm, non-tender, subcutaneous nodules which exhibited an unusual degree of mobility. As long ago as

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1912, Shaw and Hopkins¹³ had reported a patient with Ehlers-Danlos syndrome who had hard, movable subcutaneous nodules which they considered to be fibromata or neuromata. In discussing this paper, Weber told how Morris in 1900 had biopsied a similar lesion in another patient with hyperelastic skin. The nodule "seemed to consist of a spherical fibrous outer portion (in which was possibly a zone of calcification) and a fluid inner portion." Morris' patient and 2 others with similar changes were reviewed by Weber¹⁶ in 1923. Fifteen years later, Weber and Aitken^{17,18} described in great detail a patient of their own in whom they had observed subcutaneous "spherules" associated with the original Ehlers-Danlos signs.

Whereas Weber and Aitken supported the idea of Tobias that the peculiar subcutaneous nodules represent a fifth component of the syndrome in certain cases, they did not concur in his explanation of the nature of these lesions. They described the nodules as shot-like, oil-containing cysts surrounded by fibrous or calcified capsules. Presumably the nodules resulted from localized avascular degeneration of adipose tissue with subsequent repair.

It is the "fifth sign" of the Ehlers-Danlos syndrome which is of particular importance to radiologists. Our interest in the condition was kindled recently by the observation of disseminated soft tissue calcium deposits in the extremities of two sisters presenting typical clinical signs of the syndrome. This interest was intensified by a review of the literature on the subject which revealed that no roentgenograms illustrating the calcified subcutaneous nodules appear to have been published. Several reports included roentgenograms of the hands and wrists for the purpose of demonstrating hyperflexibility of the joints. In a few articles it was stated that roentgen examination of the long bones had shown no abnormality. Bolam,¹ in describing the case of a fourteen year old boy, mentioned that "on x-ray, many circular shadows could be seen and the report suggested a

slight degree of calcification at these sites." No other reference to positive roentgen findings could be found.

CASE REPORTS

The roentgenographic features observed in the case of two sisters who belong in the Ehlers-Danlos category are herewith presented. A more comprehensive study including dermatological and genetic considerations will be reported elsewhere by Johnson and Falls.⁷

CASE 1. V.M.E., a white girl, aged eighteen, was first seen in the Dermatological Out-Patient Department of the University Hospital on May 11, 1944, where the diagnosis of Ehlers-Danlos syndrome was made by Dr. Sture Johnson. The patient was referred to the Department of Roentgenology for examination of the spine and wrists because she complained of pain between the shoulder blades and numbness of the fingers.

The cervical and thoracic portions of the spine appeared normal. The distal end of the left radius was deformed slightly and surrounding soft tissues contained several small, rounded deposits of calcification. Additional roentgenograms of the entire left arm were requested to determine the extent of the soft tissue lesion which was thought to be a hemangioma producing bone erosion. This examination showed widespread calcium deposits extending all the way to the shoulder, and since there were no clinical signs of angioma, roentgenograms of the entire body were made to determine whether subcutaneous calcium deposits were widespread. Incidentally, while films were being exposed, the left sleeve of the patient's gown caught in the railing of the tube stand. Apparently the underlying skin was pinched slightly and although the patient complained of no pain whatsoever, a sizable wound resulted, necessitating immediate emergency care for control of bleeding.

Comment. Roentgenograms of all four extremities show striking soft tissue abnormality consisting of disseminated, small, rounded, discrete, calcareous nodules. These appear to involve either the skin itself or the immediate underlying tissues (Fig. 1). In the upper extremities these calcifications are seen to be largest and

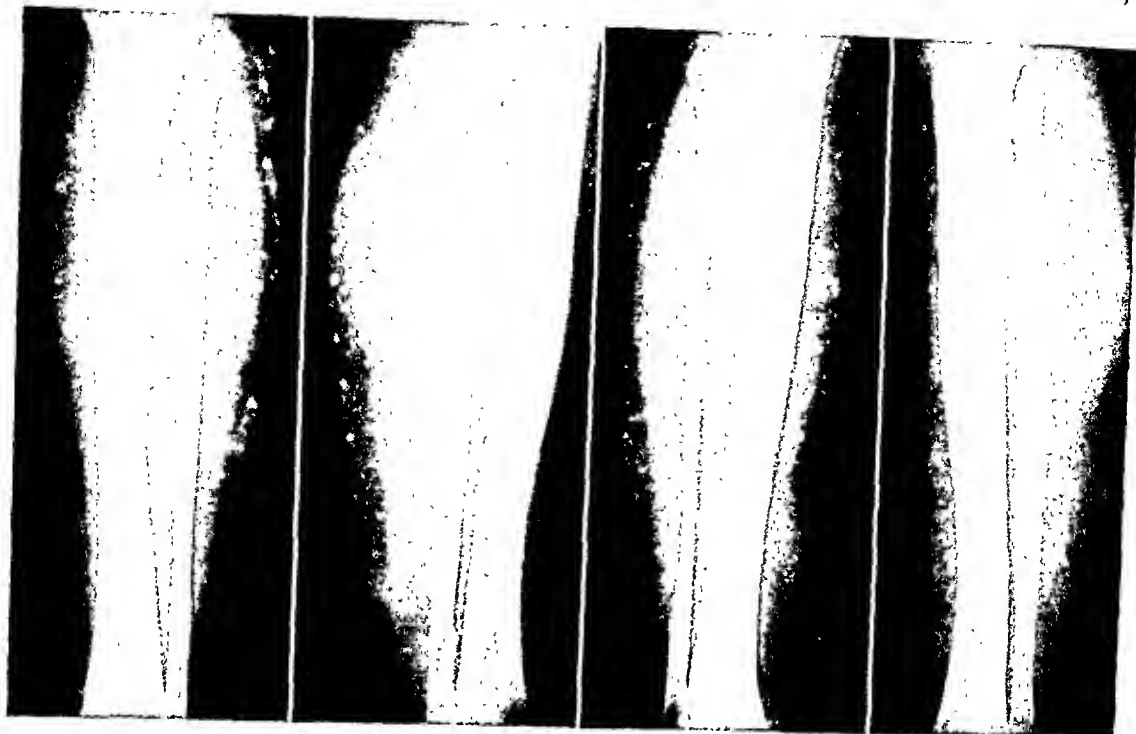


FIG. 1. Case 1. Calcified subcutaneous lobules of fat in Ehlers-Danlos syndrome. Distribution is bilaterally symmetrical and largely superficial. Wavy irregularity of skin surface is due to traumatic hematomata (pseudotumors).

most numerous on the extensor surfaces, being particularly abundant over the lower deltoid regions (Fig. 2). A few scattered nodules are evident on the medial aspect of the upper arm, but the flexor surfaces of the forearm are entirely normal in appearance.

Involvement of the thighs is limited almost exclusively to the extreme lateral surfaces, with distribution around the greater trochanteric regions being somewhat more generalized but always superficial.

By far the greatest concentration of calcified "spherules" is present in the lower legs. Here the lesions are more widely disseminated, although a definite predilection for the lateral and medial skin surfaces is manifested. The flexor surfaces of the knees and all of the soft tissues around the ankles for some distance above the ankle joints contain none of the concretions. No nodules are found about the distal portions of the forearms, the wrists, hands, feet, scalp or trunk.

At first glance it appears that the pattern of skin calcification conforms to those portions of the extremities most subject to trauma, but this is true only where there is an appreciable amount of adipose tissue. Thus, there are numerous calcium deposits over the hips and upper arms, but the elbows, knees and ankles show little or no involvement. In direct contradistinction, the larger pseudotumors are most prominent around the joints.

Individually, the subcutaneous calcium deposits have a rather constant appearance (Fig. 2). In most instances, a central zone of relatively increased radiolucency is surrounded by a ring-like shadow of lime salt. Some of the nodules are faintly stippled and a few are entirely homogeneous, but these are in the minority.

Case II. V. E., a white girl, aged sixteen, was sent to the University Hospital Bone and Joint Department on April 20, 1944, for treatment of a tumor involving her left knee. Roentgenographic signs of primary malignant neoplasm of the proximal portion of the left tibia were

confirmed by biopsy. The tumor was an osteochondrosarcoma.

Unknown to the Department of Roentgenology, the patient was referred to Dermatology because peculiar hyperelasticity of her skin had been noted. Dr. Sture Johnson made a diagnosis of Ehlers-Danlos syndrome. When the roentgenologic signs, already described, had been observed in Case I, the leg roentgenograms showing the bone tumor (Case II) were reviewed



FIG. 2. Case 1. Prominent collection of nodules over left deltoid insertion. Dense outer margins and relatively radiolucent centers characterize most of the lesions.



FIG. 3. Case 11. Ehlers-Danlos syndrome. (Roentgenogram of surgical specimen. Left leg amputated because of osteochondrosarcoma, upper end of tibia.) Small calcified nodules can be seen on lateral aspect of leg.

but, because heavy exposure had been used to show bone detail, superficial tissues could not be seen clearly. Subsequent supracondylar amputation of the patient's left leg, however, afforded a splendid opportunity to scrutinize the calcified nodules more closely from both the roentgenologic and pathologic aspects.

Roentgenograms of the surgical specimen, lightly exposed, showed only a fraction of the great number of calcified subcutaneous nodules observed in the extremities of the patient's sister, but nevertheless they were of the same general configuration and distribution (Fig. 3).

Gross pathologic examination of the amputated leg (exclusive of the tibial neoplasm) showed the skin to be very hyperelastic with "peculiar scarring over the prominences." There were many subcutaneous nodules varying from the size of a millet seed to a pea, some of which were obviously calcified. Histopathologically, these concretions proved to be partially calcified lobules of subcutaneous fat (Fig. 4).

Comment. Microscopic review of the subcutaneous concretions in this patient reveals several features of considerable

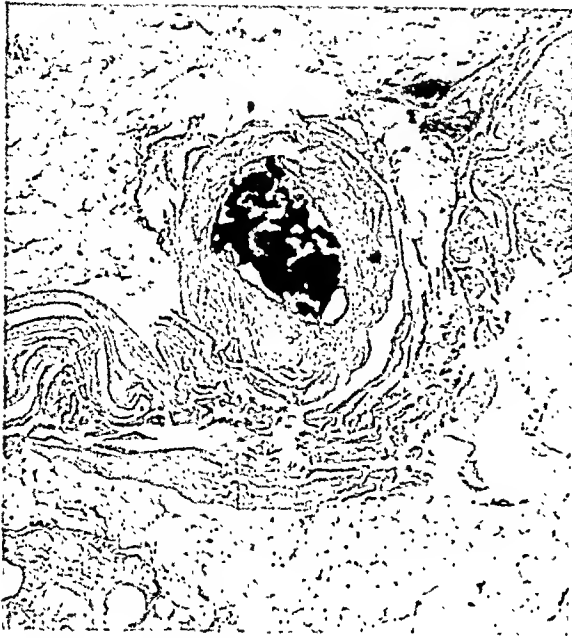


FIG. 4. Case 11. Low power microscopic section of typical subcutaneous nodule. Calcified necrotic fat (center) is surrounded by collagenous fibrous tissue capsule.

interest. Only a small percentage of the total number of nodules contain any calcium deposition whatsoever, the majority consisting of isolated groups of fat cells tightly compressed within collagenous fibrous capsules of varying thickness. A few of the fat cells have normal appearing nuclei, but for the most part they are definitely necrotic, and it is within this tissue that calcium is deposited. Occasional foreign body giant cells are seen dispersed throughout the necrotic fat. Uniform increase in elastic tissue is clearly evident in the corium.

The ring-like peripheral density observed roentgenographically in many of the larger nodules is somewhat difficult to rationalize on the basis of the microscopic findings which show the lime salt to be located centrally. It should be remembered, however, that some of the smaller nodules have a more homogeneous density and these are undoubtedly the ones from which histologic sections were made. Apparently in the case of the larger nodules, calcification is most pronounced just inside the fibrous outer

capsule, with the central portion consisting largely of radiolucent non-calcified fat.

The etiology of the subcutaneous nodules in the Ehlers-Danlos syndrome is open to considerable speculation. The opposing views of Weber and Aitken, Tobias, and Shaw and Hopkins have already been mentioned and certainly additional opinions have been expressed in the past. It may well be that trauma plays more than a minor rôle in the formation of these lesions. The presence of necrotic fat and foreign body giant cells within the nodules as well as the distribution of these "spherules" on the extensor surfaces of the extremities tend to support such an explanation.

As has been suggested, the calcified nodules superficially resemble the more commonly encountered phleboliths in hemangiomata. Adding to the confusion is the fact that the entirely independent pseudotumors of the Danlos syndrome and the



FIG. 5. Calcified hemangiomatous phleboliths in forearm of two different patients. Note similarity to subcutaneous nodules in Ehlers-Danlos syndrome (Fig. 1, 2 and 3).

irregular tumor masses of sizable angiomas present much the same roentgenographic appearance. Furthermore, both entities are sometimes associated with minor alterations of normal bone architecture. Fortunately, the clinical differentiation of the two conditions is relatively simple and careful correlation of clinical and roentgen findings will avoid any serious confusion in diagnosis.

Some of the roentgenographic features of angiomatous phleboliths actually are rather distinctive and may assist materially in differentiating these vascular calcifications from the calcified Ehlers-Danlos nodules. Whereas the latter are entirely superficial in location, phleboliths are apt to be distributed throughout the deeper soft tissues. Phleboliths show more variation in size, are more irregular in outline, and contain multiple concentric strata of calcium which give the individual concretions a crystal-like appearance (Fig. 5).

The larvae of parasites such as *Cysticercus cellulosae* may calcify in the muscles of the extremities and produce roentgenologically visible shadows which are vaguely similar to those described in conjunction with the Ehlers-Danlos syndrome. Recognition of peculiarities of shape, and due attention to clinical and laboratory data aid in their proper identification.

The far more common forms of soft tissue calcification either appear as solitary lesions or occur in such an amorphous fashion that they offer no serious differential diagnostic difficulties.

SUMMARY

1. The Ehlers-Danlos syndrome is well established on the basis of clinical findings consisting of hyperelasticity and hyperfragility of the skin, hypermobility of the joints and the formation of pseudotumors, papyraceous scars and numerous subcutaneous nodules.

2. The subcutaneous nodules, confined to the extremities, may calcify and become roentgenologically visible. Two sisters who

manifested these changes are presented in brief.

3. Roentgenographically, the calcified nodules may be confused with the more commonly encountered phleboliths in hemangiomata. The differentiating features of these two entities are considered.

4. Histopathologically, the Ehlers-Danlos nodules consist of lobules of calcified, necrotic fat surrounded by dense fibrous tissue capsules.

5. Repeated trauma may be an important etiologic factor.

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A QUANTITATIVE ROENTGENOGRAPHIC METHOD FOR THE DETERMINATION OF LEFT AURICULAR SIZE NORMAL STANDARDS

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THE importance of roentgenographic evidence of enlargement of the left auricle in the diagnosis and management of rheumatic heart disease is at present generally accepted.^{4,15,18,20} Indeed, Parkinson¹⁷ and Sosman²⁵ have stated that the presence of an enlarged left auricle is second in significance only to the characteristic murmurs for the diagnosis of mitral valvular disease.

The roentgenographic findings in cases with a patently normal or markedly enlarged left auricle offer little difficulty. Numerous roentgen signs have been reported as aiding in the recognition of moderate or marked enlargement of this chamber.^{3,7,9,11,14,24,26,32} These findings, however, are not observed in cases with only slight enlargement of the left auricle, and considerable difficulty is frequently encountered in the recognition of a minimal enlargement.^{3,6,12,20,21,25} Much of this difficulty is due to the wide variation in the outline of the auricle in normal cases, and to the absence of a sharply defined difference between the appearance of the normal and minimally enlarged auricular chamber. The purpose of this paper is to demonstrate the amount of roentgenographic variation in the appearance of the left auricle in healthy individuals and to furnish quantitative standards establishing the distribution range for this normal variation. These standards, it is believed, may be of considerable value in more clearly delineating the border between the normal and slightly enlarged left auricle.

The appearance of the barium-outlined esophagus has been firmly established as one of the most accurate methods for demonstrating the left auricular contour,^{6,10,14,15,19,20,32} and has been employed

as the basis of this study. Determination of the size of the left auricle (without the aid of esophageal opacification) by the direct observation of changes in the cardiac silhouette¹³ has not been found sufficiently accurate for the diagnosis of a minimal enlargement.

NORMAL AND ABNORMAL ANATOMY, ROENTGENOGRAPHICALLY CONSIDERED

The esophagus enters the thoracic inlet slightly to the left of the midline between the trachea and the spine. It proceeds inferiorly to the level of the fifth thoracic vertebra, where it swings to the midline and continues downward and forward in this position. At a point 2 to 3 cm. above the diaphragm it turns toward the left and descends to enter the abdomen through the esophageal hiatus.^{8,20}

There are three main impressions on the opacified thoracic esophagus as seen on the oblique and lateral roentgenograms. These from above downward are (a) the aortic, (b) bronchial, and (c) left auricular. The aortic impression is seen constantly. It is caused by pressure of the posterior portion of the aortic arch on the left side of the esophagus. A short distance (average 0.7 cm.) below the lower end of the aortic indentation is the inconstant bronchial impression.^{6,7,15,20,24,27,29} When present, it may be caused by the left main bronchus, the trachea at its bifurcation or the right main bronchus, depending upon the variation of the relationship of the tracheal bifurcation to the esophagus (Fig. 1 and 8). Just below the bronchial indentation there is normally no impression on the esophagus for a distance of 1 to 8 cm. (average 2 to 5 cm.). This portion of the esophagus is designated as the segment "alpha" (Fig. 1

and 2). The region anterior to the "alpha" segment is occupied only by connective tissue and small mediastinal lymph nodes^{9,19} (Fig. 3). Immediately below the "alpha" segment the auricular impression begins and is present for a distance of 5 to 6 cm. down to a point 2 or 3 cm. above the diaphragm.

In the oblique and lateral views, the general course of the esophagus is downward and usually anterior. Less often, the esophagus may proceed downward in a truly vertical position, and infrequently, the course is downward and minimally posterior (Fig. 4). At the sites of the three main impressions, the esophagus shows local posterior bulges, but resumes its general downward and anterior direction immediately after passing the indentations. The best indicator of the general esophageal course is the direction of the "alpha" segment, located below the bronchial indentation, since there are no local impressions by adjacent viscera on this portion of the esophagus.

The angle which the posterior border of the opacified esophageal "alpha" segment makes with the vertical axis has been designated as "gamma" (Fig. 1 and 2). This angle is a measure of the direction of the "alpha" segment and therefore is an index of the general esophageal course.

At the lower end of the "alpha" segment the normal left auricular impression on the esophagus begins. The angle between a downward extension of the posterior border of the "alpha" segment and the posterior margin of the esophagus in the upper portion of the auricular impression has been designated as the angle "theta" (Fig. 1 and 2).

The anteroposterior relationship of aortic arch bulge of the esophagus to the auricular bulge varies. Usually, the aortic arch displaces the esophagus more posteriorly than does the normal left auricle. This relationship is determined as follows: From the most posterior point on the posterior border of the opacified esophageal shadow in the aortic bulge a vertical line

is dropped. The distance between this line and the most posterior point on the posterior esophageal border in the region of auricular impression is determined. This distance has been designated as "*M.P.*"; i.e., maximal posteriority of the esophageal auricular bulge in relation to the aortic impression (Fig. 1, 2 and 5). The value of "*M.P.*" depends upon three major factors. These are: (a) the general anterior (or vertical or posterior) direction the esophagus takes as it courses downward; (b) the amount of local bulging in the auricular region; (c) the amount of local bulging in the aortic arch region.

The selection of a series of quantitative indices for the determination of the left auricular size was influenced by a consideration of the changes in the appearance and size of the left auricle in cases with definite mitral disease. It was felt that strict statistical analysis of the normal variations of the indices selected and observations on abnormal cases might be of great aid in more clearly establishing the border between the normal and enlarged auricle. A brief review of some of these considerations therefore follows.

The left auricle, as it enlarges, expands in a posterior direction early in its course.^{6,9,10,16,19,20,22,25,32} Upward enlargement is usually seen shortly afterward. Enlargement to the right and left usually becomes more apparent only after the posterior expansion has been impeded by adjacent structures such as the aorta and spine. Thus, the best criteria of early enlargement appear to be posterior and upward bulging of the auricle. Since the esophagus lies adjacent the posterior wall of the left auricle, the first manifestation of enlargement should be an increase in the posterior displacement of the juxta-auricular portion of the esophagus, i.e., "*M.P.*" This posterior displacement should also be indicated, in the early phases, by an increase in the angle between the lower end of the "alpha" segment and the upper portion of the esophageal impression (i.e. the angle "theta"). With additional dilata-

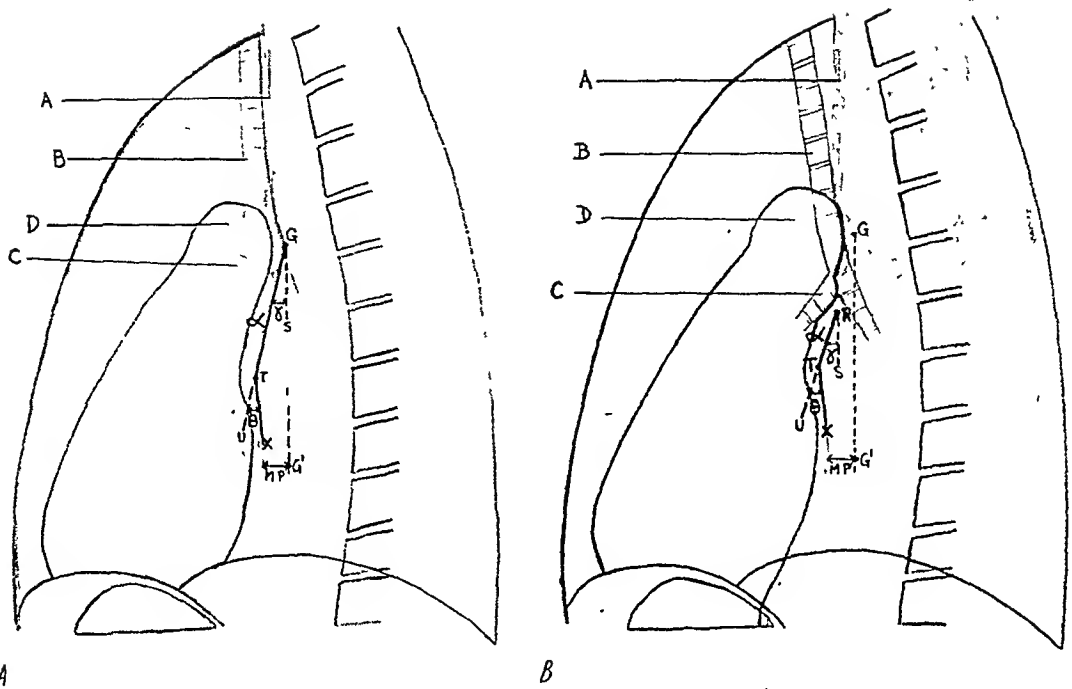


FIG. 1. Diagram of esophagus in normal case. (A) Shows no bronchial impression on esophagus. A, esophagus; B, trachea; C, left main bronchus; D, aortic arch; line GT, "alpha" segment; angle TGS, "gamma"; angle UTX, "theta"; "M.P.," distance from most posterior point on posterior border of esophagus in the auricular region to a vertical line (GG') dropped from the most posterior point on the posterior border of the esophagus in the region of the aortic knob indentation. (B) Shows esophageal impression by left main bronchus. Note that in the presence of a bronchial impression the "alpha" segment (TR) is shortened. Angle TRS, "gamma." Other identifying letters are the same as in (A).

tion, however, the auricle expands upward as well as further posteriorly, and the lower end of the "alpha" segment is seen to become displaced backward. In these cases the entire "alpha" segment then assumes a downward and posterior course rather than the usual (in the normal) downward and anterior direction. As a result, there should be noted a diminution of the angle "theta," as well as an increase in the posteriority of "M.P." and the angle "gamma." These changes actually have been found to occur before evidence of auricular enlargement to the right or left, elevation of the left main bronchus, and widening of the tracheobronchial angle appeared.

Methods were therefore employed to yield quantitative measurements for the indices of left auricular size: (1) the angle "theta," (2) "M.P.," and (3) the angle

"gamma." A series of other measurements, namely (a) height and weight relationship, (b) frontal cardiac area, (c) transverse cardiac diameter and (d) thoracic height were also made, and statistical correlations calculated between these external, somatic factors and the three main indices.

MATERIAL AND METHODS

Two hundred and fifty healthy male soldiers between eighteen and thirty years of age were selected following a detailed history, physical and electrocardiographic examination. Any evidence even slightly suggestive of rheumatic fever, heart disease, cardiac murmur, elevated blood pressure or other abnormality caused exclusion from the study. A set of four roentgenograms was obtained for each examinee, measurements were made on these roent-

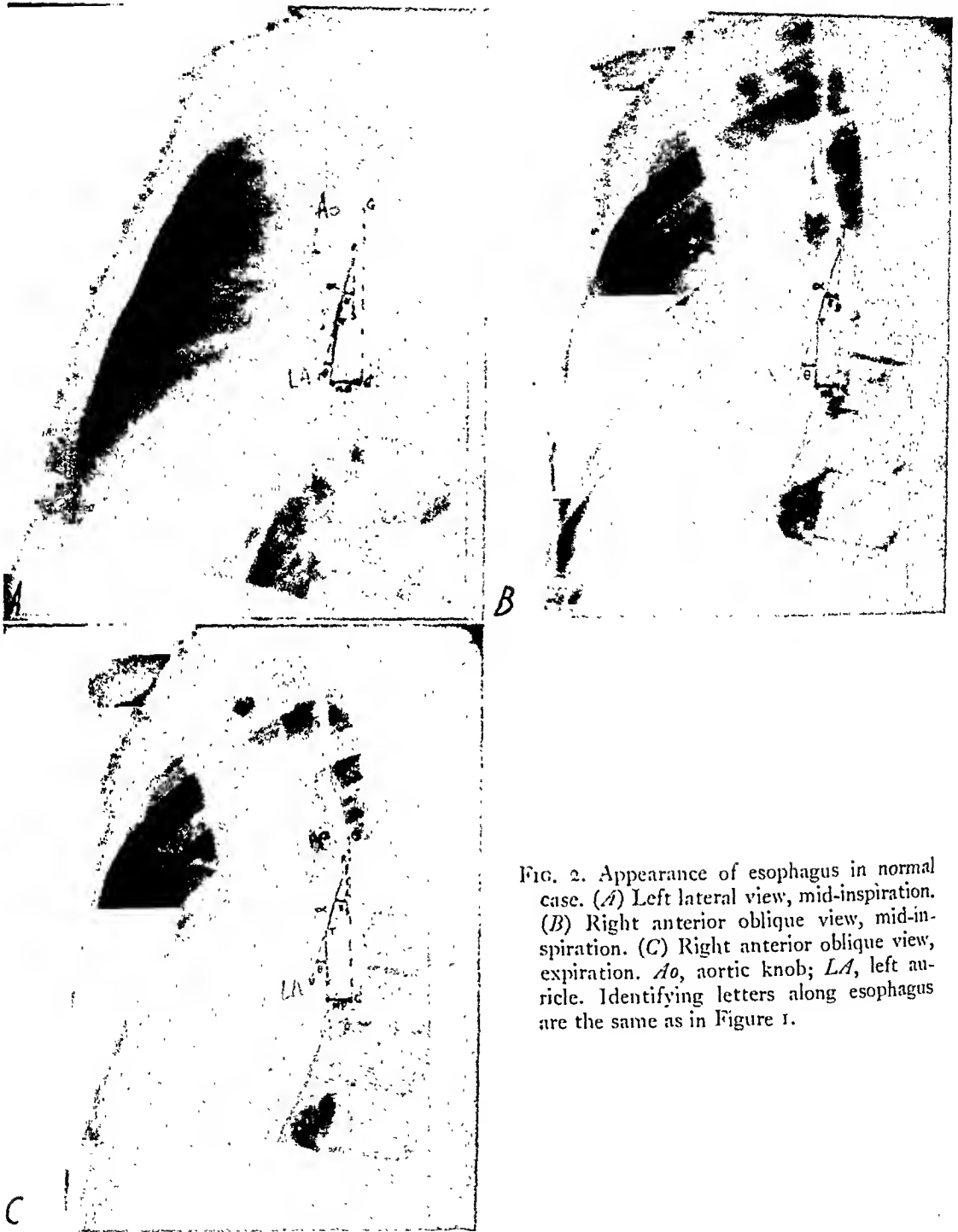


FIG. 2. Appearance of esophagus in normal case. (A) Left lateral view, mid-inspiration. (B) Right anterior oblique view, mid-inspiration. (C) Right anterior oblique view, expiration. *Ao*, aortic knob; *LA*, left auricle. Identifying letters along esophagus are the same as in Figure 1.

genograms, and a series of normal standards created.

The following views were employed in the study of each subject:

1. Posteroanterior in mid-inspiration.
2. Left lateral in mid-inspiration.

3. Right anterior oblique in mid-inspiration.
4. Right anterior oblique in expiration.

The esophagus was opacified for each of these views with the aid of a very thick

barium paste. The subject swallowed one mouthful, and about fifteen seconds later the exposure was made. In this manner, the esophagus was well outlined but not distended by the contrast material. Distention of the esophagus by the barium mixture was found to impair considerably

head and neck on the thorax was avoided. A 45° - 50° angle was employed, so that the shadow of the opacified esophagus cleared the spine. However, a variation from about 40° to 55° resulted in no significant discrepancies in the measurements, and no special apparatus was considered



Fig. 3. Cross-section of thorax (after Eycleshymer, A. C., and Shoemaker, D. M. *A Cross-Section Anatomy*. D. Appleton & Co., N. Y., 1923, pp. 63 and 65). (A) Level of D5, through "alpha" segment. Note the mediastinal lymph nodes (L.N.) and connective tissue between the esophagus (E) and the pulmonary artery (P.A.). The right and left main bronchi lie on each side of the mediastinal lymph nodes between the esophagus and pulmonary artery. (B) Level of D7, through the upper part of the base of heart. Note the close proximity of the esophagus (E) to the posterior surface of the left auricle (L.A.).

the accuracy of the measurements. Therefore, the presence of a considerably distended esophagus in any view was considered as an unsatisfactory study and required re-examination. All roentgenograms were made at a 6 foot target-film distance. Correct posturing was considered essential and each roentgenogram was made with the subject standing perfectly erect. In the oblique examinations special care was required. Both shoulders of the examinee were placed evenly, eliminating any elevation on one side. Rotation of the

necessary for accurately establishing the degree of obliquity. In the lateral view, the arms were held above the head and the subjects stood as erectly as possible. Tendency toward slouching was corrected.

Table I shows the measurements made in this study. The methods for making these measurements are as follows:

1. *Posteroanterior View*. Transverse diameter of the heart and cardiac area were measured according to the Ungerleider and Gubner³⁰ method. Results were recorded as percentile variations from the predicted

normal values found in the prediction tables created by these authors. Evidence of kyphoscoliosis was also noted.

2. Both Right Anterior Oblique Views.

(a) "M.P.," the maximal point of posteriority of the opacified esophagus in the region of the auricular impression as related to the esophagus at the aortic arch bulge. A vertical line is dropped from the most posterior point on the posterior

approximates a straight line, or at most, forms a very shallow curve. Small local variations in the curve are to be discounted. The angle is measured with a protractor.

(c) Angle "gamma." This is the angle between the posterior border of the esophageal "alpha" segment and the vertical. It is formed by dropping a vertical line from any point on the "alpha" segment,

TABLE I
MEASUREMENTS DETERMINED FROM EACH ROENTGENOGRAM

	Posteroanterior View Mid- Inspiration	Left Ventral View Mid- Inspiration	Right Anterior Oblique View Mid-Inspiration	Right Anterior Oblique View Expiration
"M. P."		×	×	×
Angle "theta"		×	×	×
Angle "gamma"		×	×	×
Thoracic height			×	×
Transverse cardiac diameter	×			
Frontal cardiac area	×			

surface of the outlined esophagus at the aortic impression downward to the region of the auricular impression on the esophagus. The distance between this line and the most posterior point on the posterior border of the juxta-auricular portion of the esophagus is then measured in millimeters. A "minus" sign is placed before the value when the auricular point is anterior to the vertical line dropped from the aortic bulge (Fig. 1 and 2). When the auricular point is posterior to the line of the aortic impression a "plus" sign is placed before the value (Fig. 4 and 5).

(b) Angle "theta" (Fig. 1 and 2). The apex of this angle is situated on the posterior border of the esophageal shadow at the point of junction between the lower end of the "alpha" segment and the beginning of the segment displaced posteriorly by the auricle. One limb of the angle is formed by a downward continuation of the posterior border of the "alpha" segment, the second limb by the posterior border of the upper half of the juxta-auricular segment, which

since the value of "gamma" will be the same for any series of verticals dropped from any series of points on the segment. A point should be chosen where the posterior esophageal border is most clearly visualized and best represents the course of the "alpha" segment. The vertical limb may be obtained by drawing a line parallel with the long edge of the 14 by 17 inch film, or perpendicular to the short edge. The angle is measured with a protractor. In cases where the downward course of the "alpha" segment is anterior to the vertical line a "minus" sign is placed before the value of the angle (Fig. 1 and 2). Where the "alpha" segment proceeds downward posterior to the vertical line a "plus" sign is placed before the value of the angle (Fig. 5).

(d) Thoracic height. This is taken as the distance between the highest level of the diaphragm (right or left) and the inferior margin of the left first rib posteriorly adjacent the spine. The measurement is made in centimeters.

3. Left Lateral View.

(a) The angles "theta" and "gamma" and the distance "M.P." are measured in the same manner as in the oblique examinations (Fig. 2).

(b) Thoracic height is not measured in

periphery. With it, the angles may be measured directly and quickly from the roentgenogram. (2) A cleared, transparent 14 by 17 inch film on which vertical lines parallel to the long side and 1 cm. apart have been accurately etched. This trans-

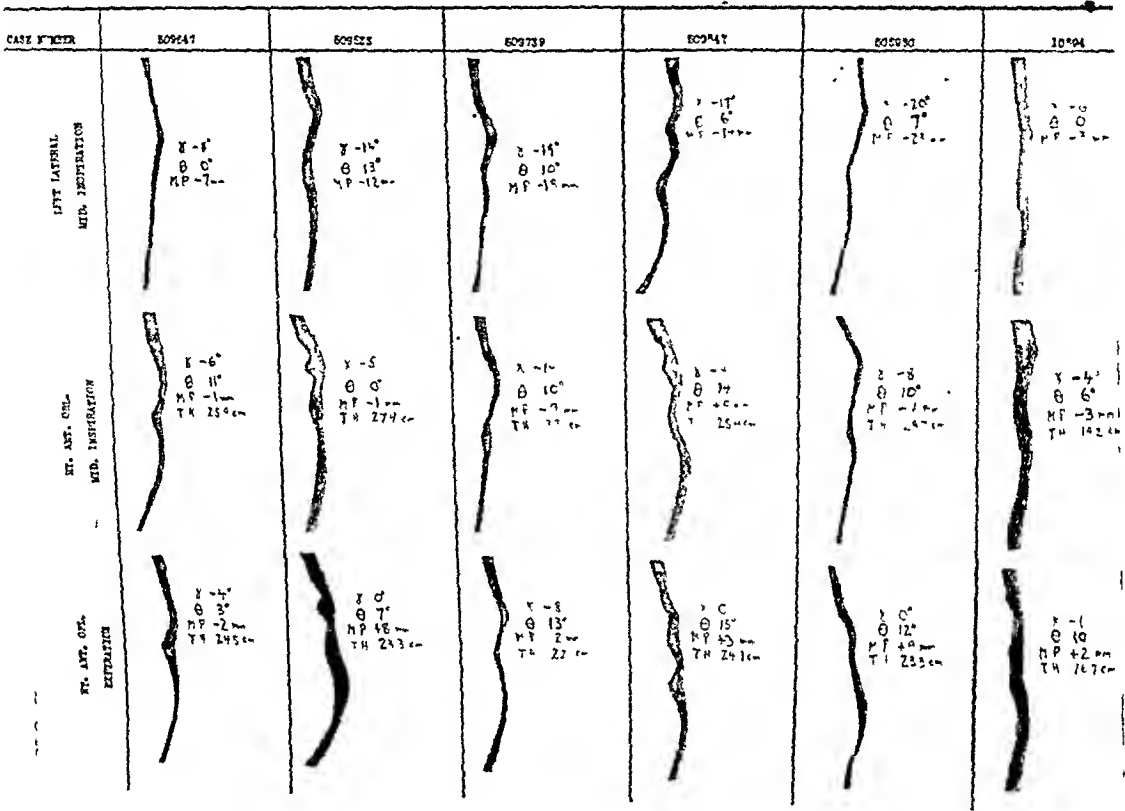


FIG. 4. Diagrams illustrating variations in the appearance of the esophagus in 6 normal cases. The index measurements are presented by the side of each drawing. The measurements for "M.P." are those prior to correction.

this view since the upper ribs cannot be clearly delineated.

4. Other Measurements.

(a) The height and weight of each subject are obtained and compared to a standard chart³¹ to determine the variation from the average of each subject's weight for his height; i.e., habitus.

(b) The age of each subject is recorded.

Two simple measuring aids (Fig. 6) have been found extremely useful. These are:

(1) A transparent protractor with a movable arm extending from its center outward over the graduated arc of its

parency is carefully inserted and cemented into a rigid frame so that the lines are absolutely parallel with the long axis of the frame. The film in its frame is then set on a view box (best lying horizontal) and the heart roentgenogram being studied is placed over the transparency so that the entire long side of the heart roentgenogram is in closest apposition with the frame. As a result, a series of vertical lines 1 cm. apart are superimposed upon the heart roentgenogram, and all measurements requiring the use of these lines are greatly facilitated.

TABLE II
INTERCORRELATIONS*

	"M. P."	"Gamma"	"Theta"
Left Lateral View, Mid-Inspiration			
Thoracic height	-.17**	—	—
Transverse diameter	-.01	-.08	.10
Frontal area	-.03	-.08	.00
Habitus	.15	.03	.12
"M. P."	—	.68	.07
"Gamma"	.68	—	-.28
"Theta"	.07	-.28	—
Right Anterior Oblique View, Mid-Inspiration			
Thoracic height	-.23	-.14	-.17
Transverse diameter	.09	.07	.16
Frontal area	.09	.04	.02
Habitus	.06	.00	.15
"M. P."	—	.74	.03
"Gamma"	.74	—	.18
"Theta"	.03	-.18	—
Right Anterior Oblique View, Expiration			
Thoracic height	-.38	-.21	-.22
Transverse diameter	.18	.05	.13
Frontal area	.14	.08	.10
Habitus	.18	.03	.15
"M. P."	—	.71	.22
"Gamma"	.71	—	-.24
"Theta"	.22	-.24	—

* The number in each box represents the correlation coefficient (r) between the two variables correlated. The 1% level of significance for $r = .16$. The 5% level of significance for $r = .12$.

** Since thoracic height could not be measured accurately in this view, the value shown represents the correlation coefficient between "M.P." and the thoracic height measured on the right anterior oblique roentgenogram made during mid-inspiration.

STATISTICAL ANALYSIS AND RESULTS

The three important indices for determining the size of the left auricle were "gamma," "theta" and "M.P." However, it was recognized that each of these three indices might be affected not only by the size of the left auricle but also by extra-auricular factors. In order to utilize the indices as accurate indicators of auricular size, any considerable influence on the measurements by extra-auricular causes (i.e. thoracic height, examinee's weight, height, etc.) had to be eliminated. Therefore, a series of intercorrelation analyses was made between each of the three indices, and between them and all possible extra-auricular factors in each of the three views. The Pearson Product-Moment* correlation method² was employed, and the coefficient of correlation of the three indices to each other and to each of the independent extra-auricular variables in the 250 normal controls was calculated (Table II). Where the correlations were small (i.e., below the 1 per cent level of significance), the extra-auricular factors were considered as not affecting the indices' measurements of left auricular size and were disregarded. On the other hand, where the correlation coefficients were large, the extrinsic factors obviously would influence the measurements and impair the indices' accuracy as indicators of auricular size. In these instances, the measurements were corrected according to the multiple, linear regression technique,¹ and the effect of the extra-auricular factors was eliminated. Following this necessary adjustment, the values could be considered accurate indicators of the size of the left auricle. The final, accurate values for "gamma," "theta" and "M.P." were then arranged in frequency distributions according to magnitude and percentile tables constructed (Table VI). These

* The formula for Pearson-Moment Method is: $r_{xy} = \frac{\sum xy}{\sigma_x \sigma_y N}$ Where

r_{xy} = coefficient of correlation between x and y
 N = number of cases
 x = deviation of the raw score, x , from mean of \bar{X}
 y = deviation of raw score, y , from mean of \bar{Y}
 σ_x = standard deviation of X
 σ_y = standard deviation of Y